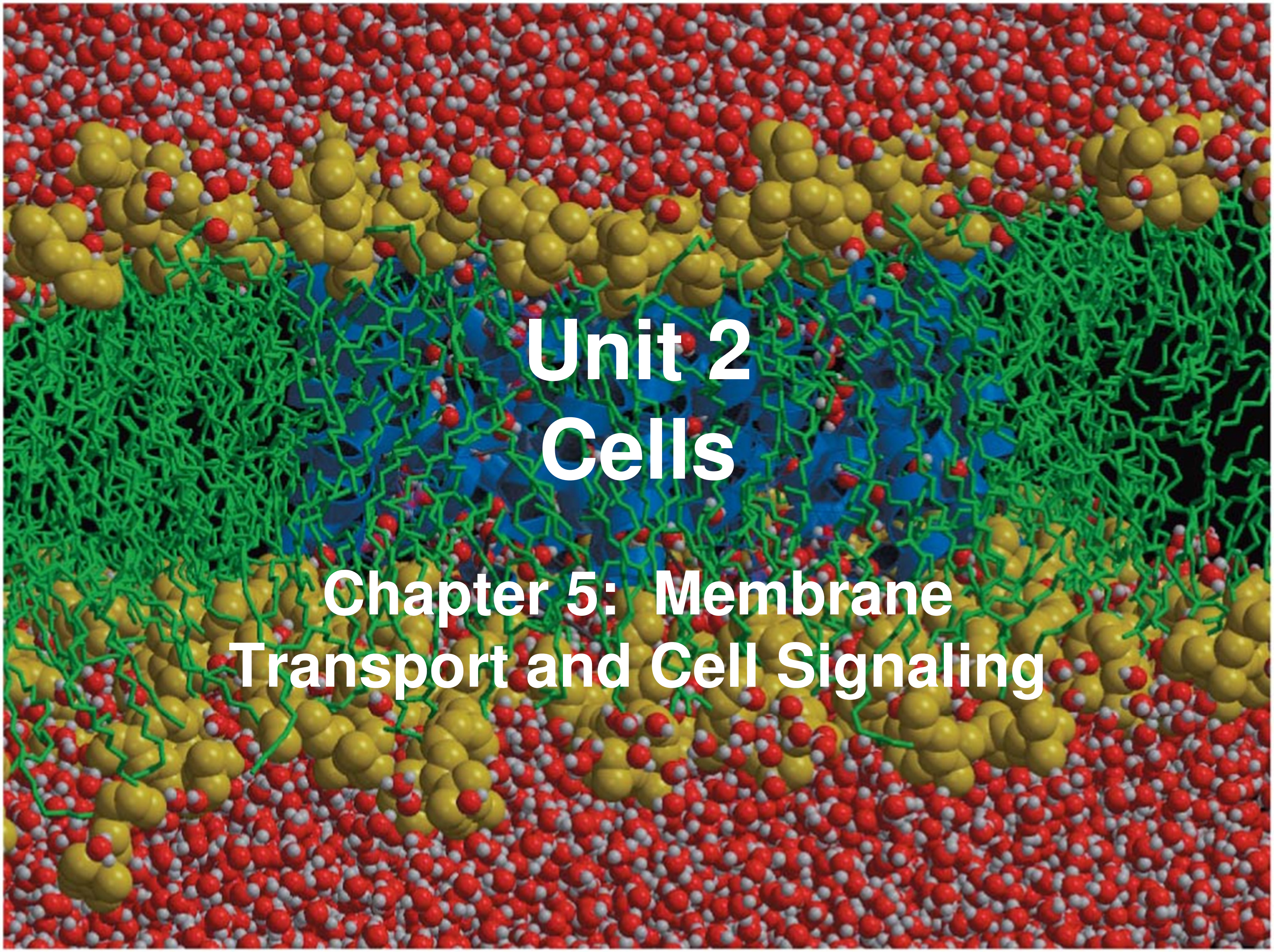
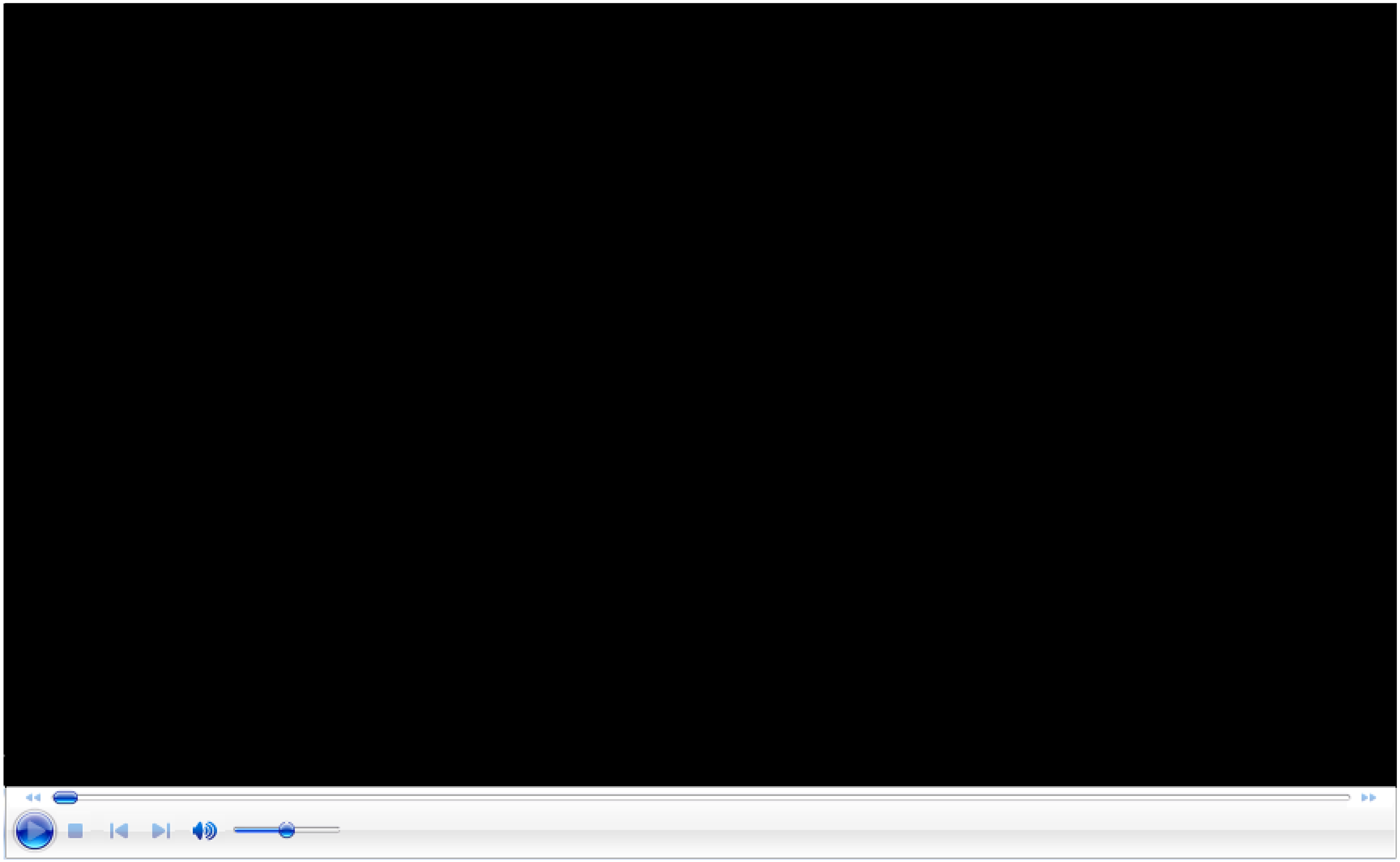


Unit 2
Cells

Chapter 5: Membrane Transport and Cell Signaling

Overview: Life at the Edge

- The plasma membrane separates the living cell from its surroundings
- The plasma membrane exhibits **selective permeability**, allowing some substances to cross it more easily than others

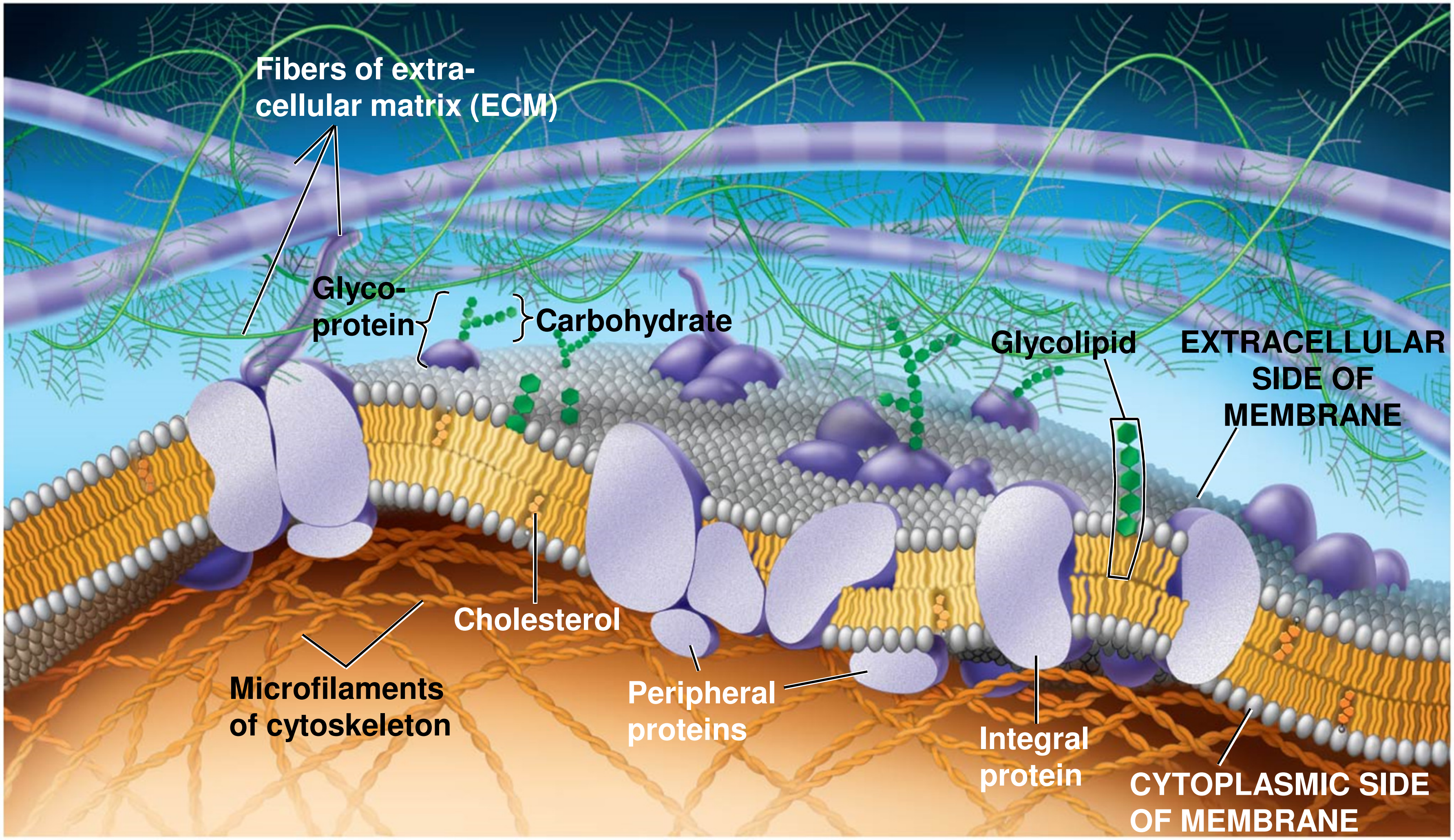


Video: Membrane and Aquaporin

CONCEPT 5.1: Cellular membranes are fluid mosaics of lipids and proteins

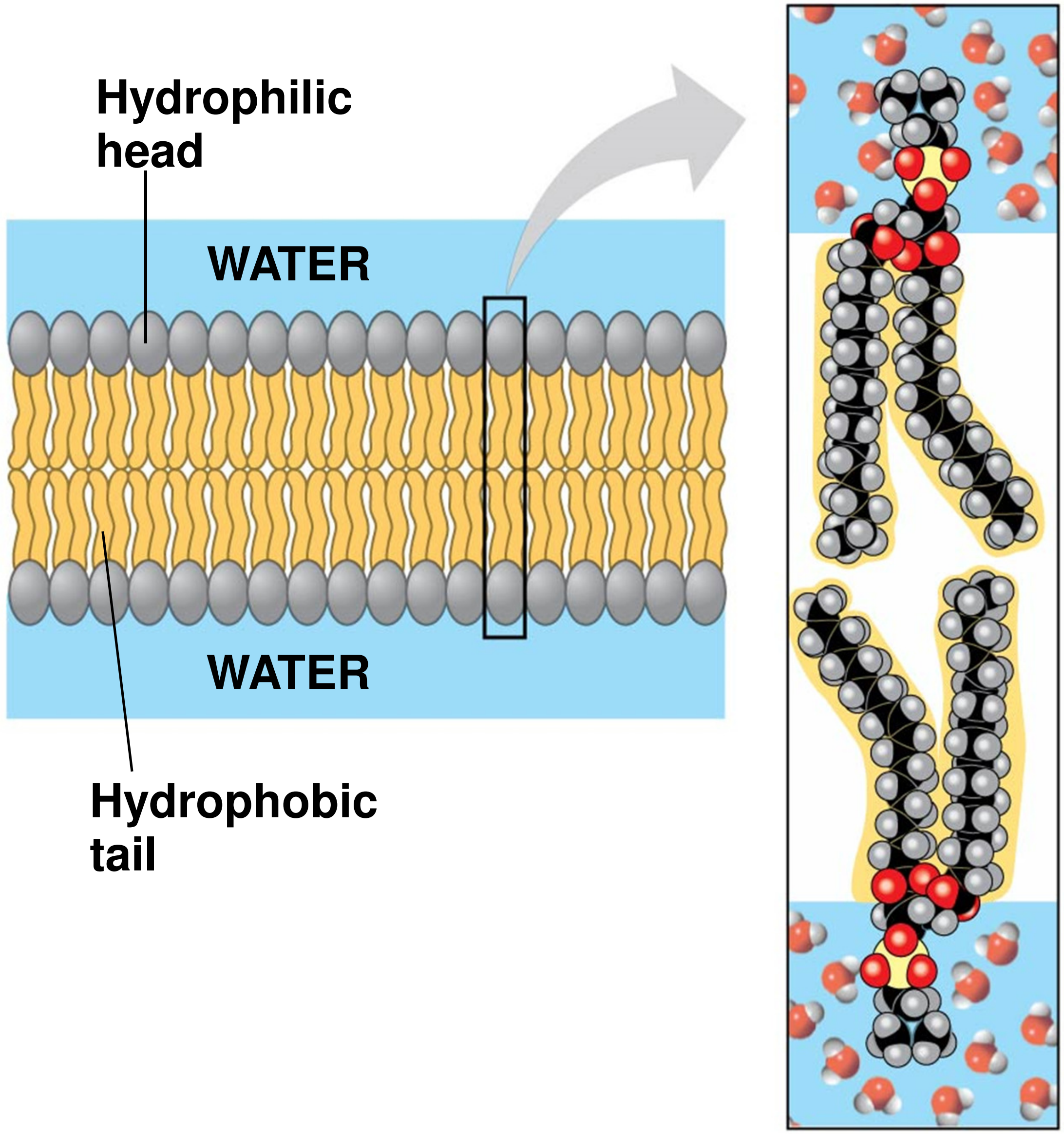
- Lipids and proteins are the staple ingredients of membranes
  - Carbohydrates are important as well
- Phospholipids are the most abundant lipid in most membranes
- Phospholipids are **amphipathic molecules**, containing both hydrophobic and hydrophilic regions
- The **fluid mosaic model** states that the membrane is a mosaic of protein molecules bobbing in a fluid bilayer of phospholipids

Figure 5.2



Fibers of extra-
cellular matrix (ECM)
Glyco-
protein
Carbohydrate
Glycolipid
EXTRACELLULAR
SIDE OF
MEMBRANE
Cholesterol
Microfilaments
of cytoskeleton
Peripheral
proteins
Integral
protein
CYTOPLASMIC SIDE
OF MEMBRANE

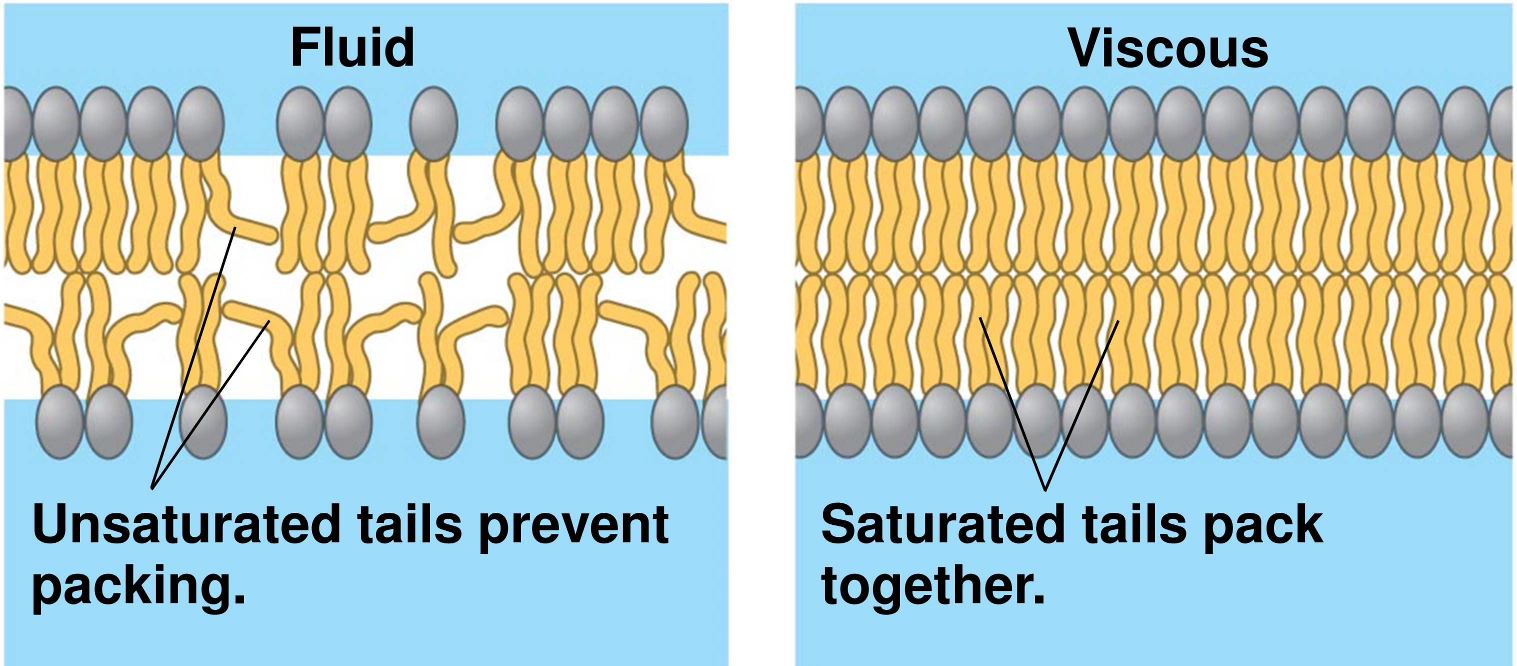
Figure 5.3



The Fluidity of Membranes

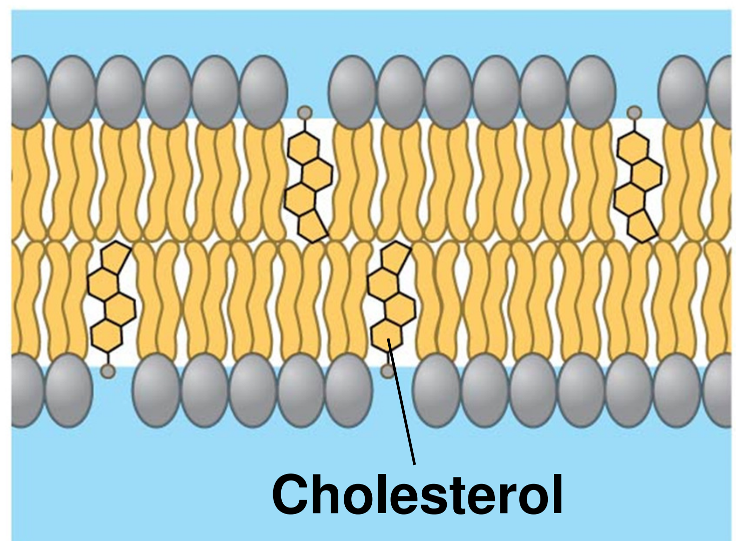
- Most of the lipids and some proteins in a membrane can shift about laterally
- Membranes must be fluid to work properly; they are usually about as fluid as salad oil
  - As temperatures cool, membranes switch from a fluid state to a solid state
  - A membrane remains fluid to a lower temperature if it is rich in phospholipids with unsaturated hydrocarbon tails
- Cholesterol helps membranes resist changes in fluidity when temperature changes
- Natural selection favors organisms whose mix of membrane lipids ensures an appropriate level of membrane fluidity for their environment

Figure 5.5



(a) Unsaturated versus saturated hydrocarbon tails

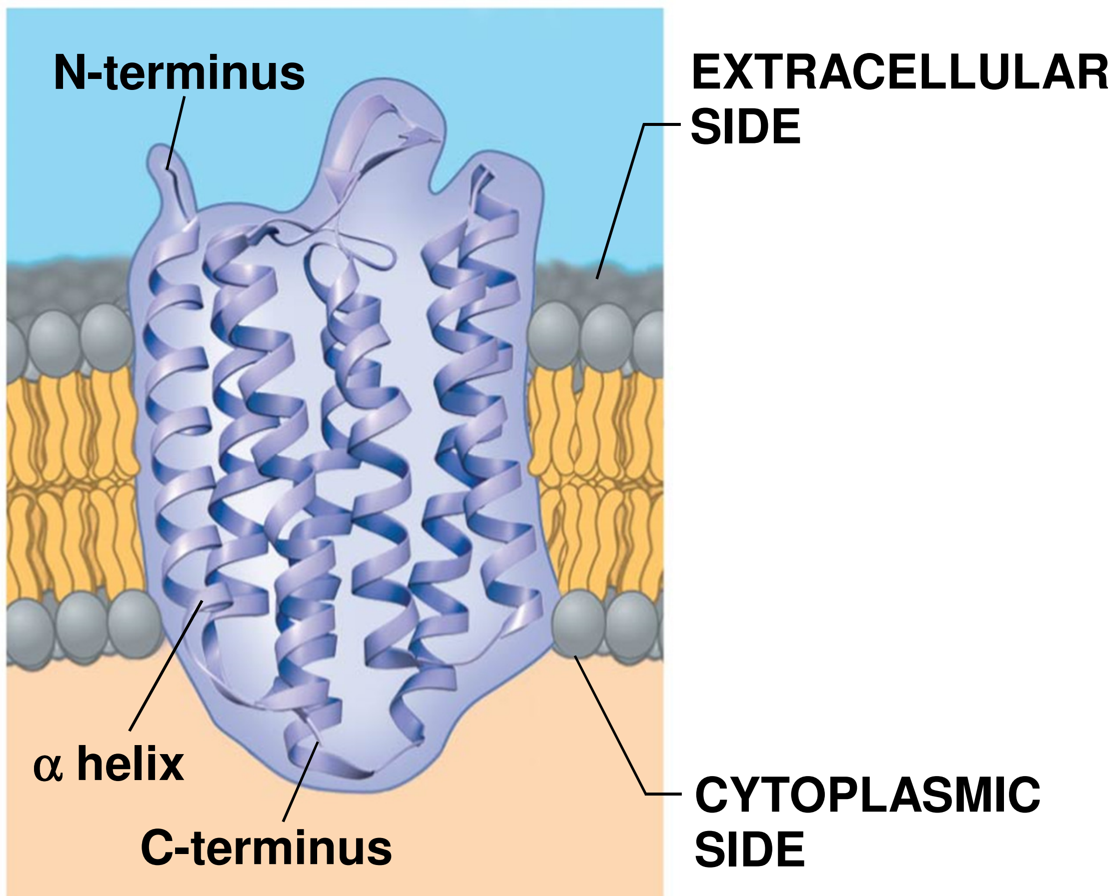
(b) Cholesterol reduces membrane fluidity at moderate temperatures, but at low temperatures hinders solidification.



Membrane Proteins and Their Functions

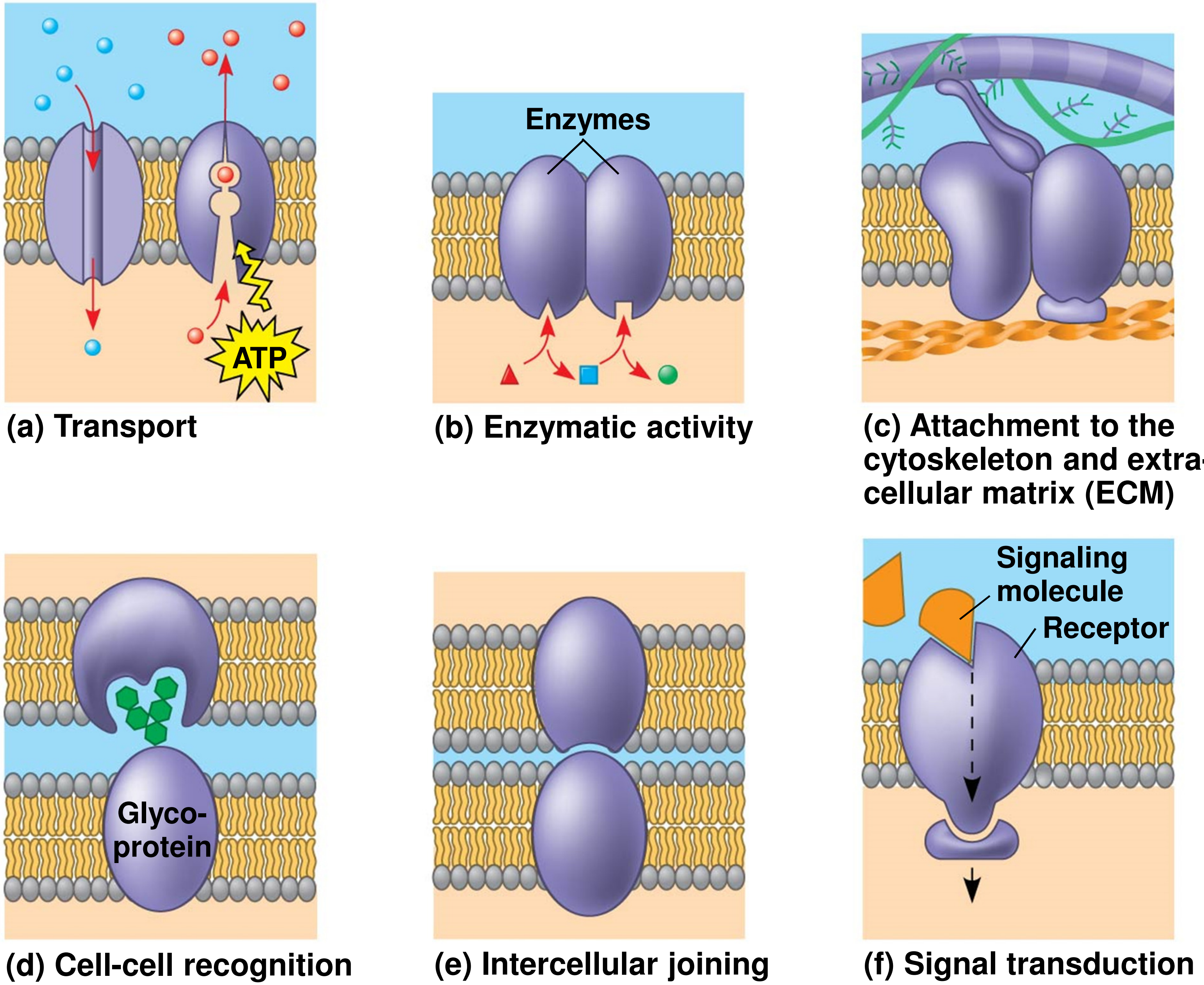
- Phospholipids form the main fabric of the membrane
- But proteins determine most of the membrane's specific functions
  - **Integral proteins** penetrate the hydrophobic interior of the lipid bilayer
    - Integral proteins that span the membrane are called transmembrane proteins
  - **Peripheral proteins** are loosely bound to the surface of the membrane

Figure 5.6


N-terminus
EXTRACELLULAR SIDE
α helix
C-terminus
CYTOPLASMIC SIDE

- Six major functions of membrane proteins
  - Transport
  - Enzymatic activity
  - Attachment to the cytoskeleton and extracellular matrix (ECM)
  - Cell-cell recognition
  - Intercellular joining
  - Signal transduction

Figure 5.7



ATP
Enzymes
Signaling molecule
Receptor
Glyco-protein
(a) Transport
(b) Enzymatic activity
(c) Attachment to the cytoskeleton and extra-cellular matrix (ECM)
(d) Cell-cell recognition
(e) Intercellular joining
(f) Signal transduction

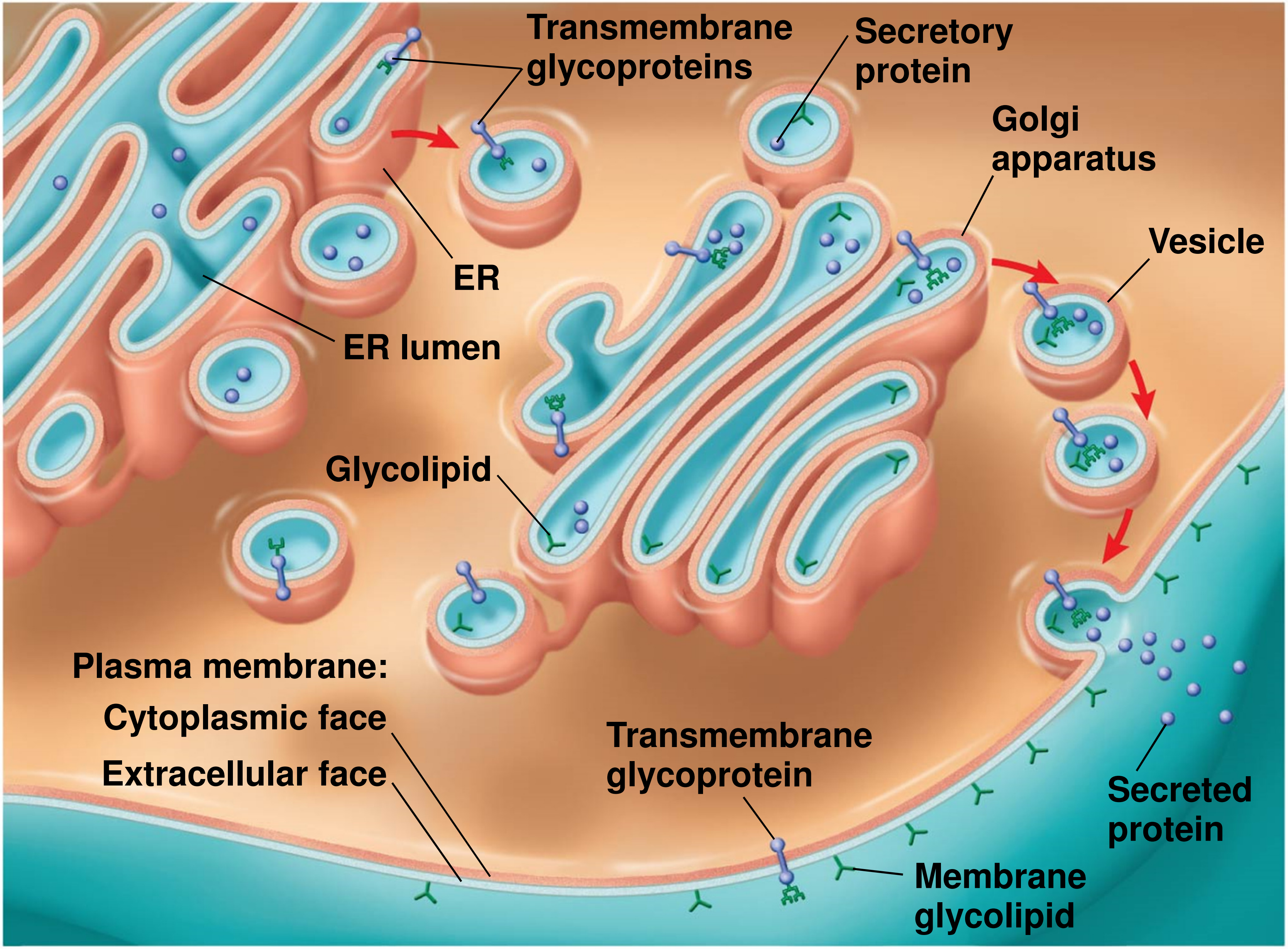
The Role of Membrane Carbohydrates in Cell-Cell Recognition

- Ability of cells to distinguish one type of neighboring cell from another (cell-cell recognition) is crucial to the functioning of an organism
- Cells recognize each other by binding to surface molecules, often containing carbohydrates, on the extracellular surface of the plasma membrane
- Membrane carbohydrates may be covalently bonded to lipids (forming **glycolipids**) or, more commonly, to proteins (forming **glycoproteins**)
  - 4 Blood Types (A, B, AB, O) reflect variation in carbohydrate part of glycoproteins on surface of red blood cells

Synthesis and Sidedness of Membranes

- Membranes have distinct inside and outside faces
- The asymmetrical distribution of proteins, lipids, and associated carbohydrates in the plasma membrane is determined when the membrane is built by the ER and Golgi apparatus

Figure 5.8


Transmembrane
glycoproteins
Secretory
protein
Golgi
apparatus
Vesicle
ER
ER lumen
Glycolipid
Plasma membrane:
Cytoplasmic face
Extracellular face
Transmembrane
glycoprotein
Secreted
protein
Membrane
glycolipid

CONCEPT 5.2: Membrane structure results in selective permeability

- A cell must regulate transport of substances across cellular boundaries
- Plasma membranes are selectively permeable, regulating the cell's molecular traffic

The Permeability of the Lipid Bilayer

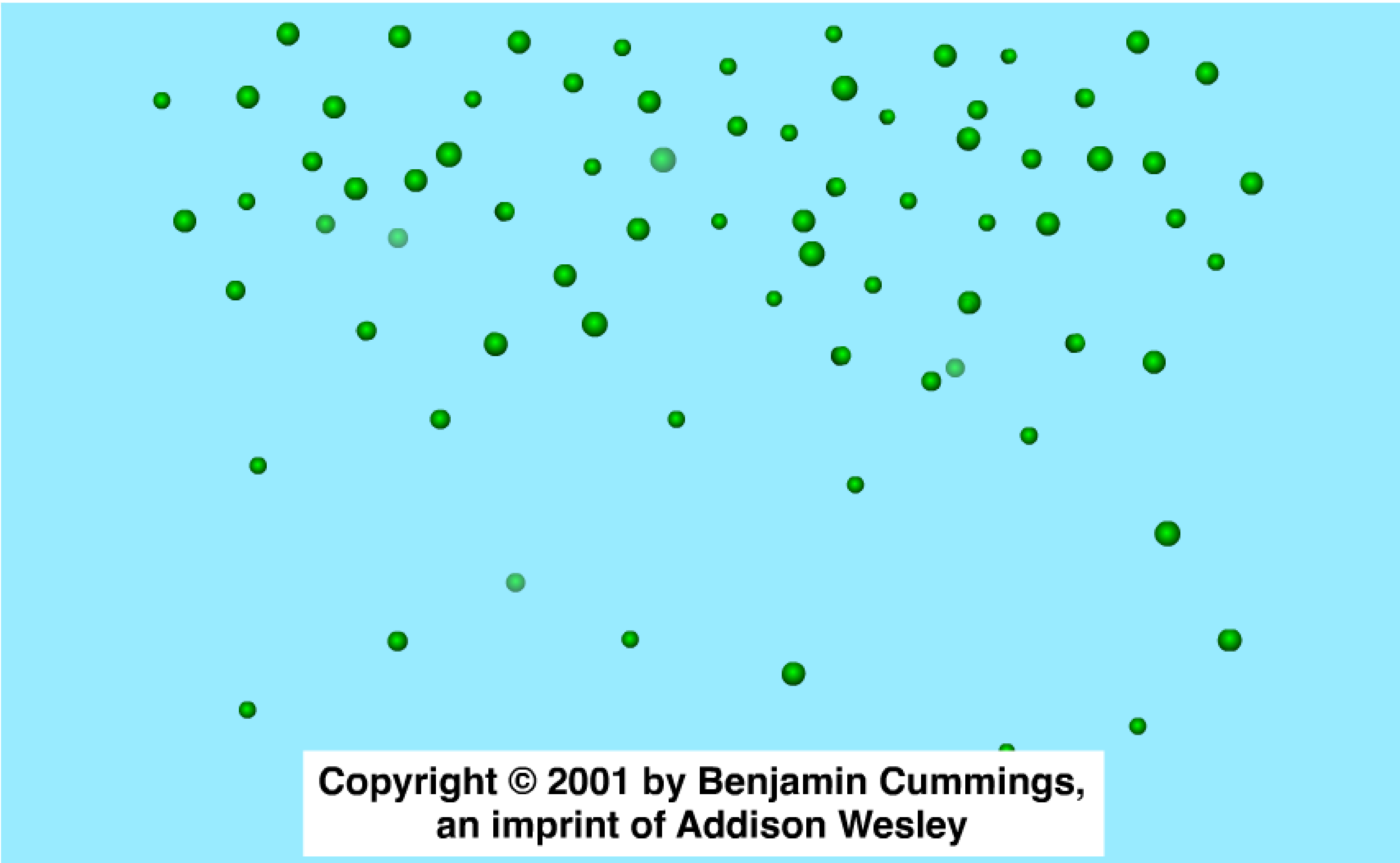
- Hydrophobic (nonpolar) molecules can dissolve in the lipid bilayer of the membrane and cross it easily
  - Hydrocarbons
  - Carbon dioxide
  - Oxygen
- Ions and polar molecules, such as sugars, which are hydrophilic do not cross the membrane easily

Transport Proteins

- **Transport proteins** allow passage of hydrophilic substances across the membrane
  - Some transport proteins, called *channel proteins*, have a hydrophilic channel that certain molecules or ions can use as a tunnel
    - Channel proteins called **aquaporins** facilitate the passage of water
  - Other transport proteins, called *carrier proteins*, bind to molecules and change shape to shuttle them across the membrane
- A transport protein is <u>specific</u> for the substance it moves

CONCEPT 5.3: Passive transport is diffusion of a substance across a membrane with no energy investment

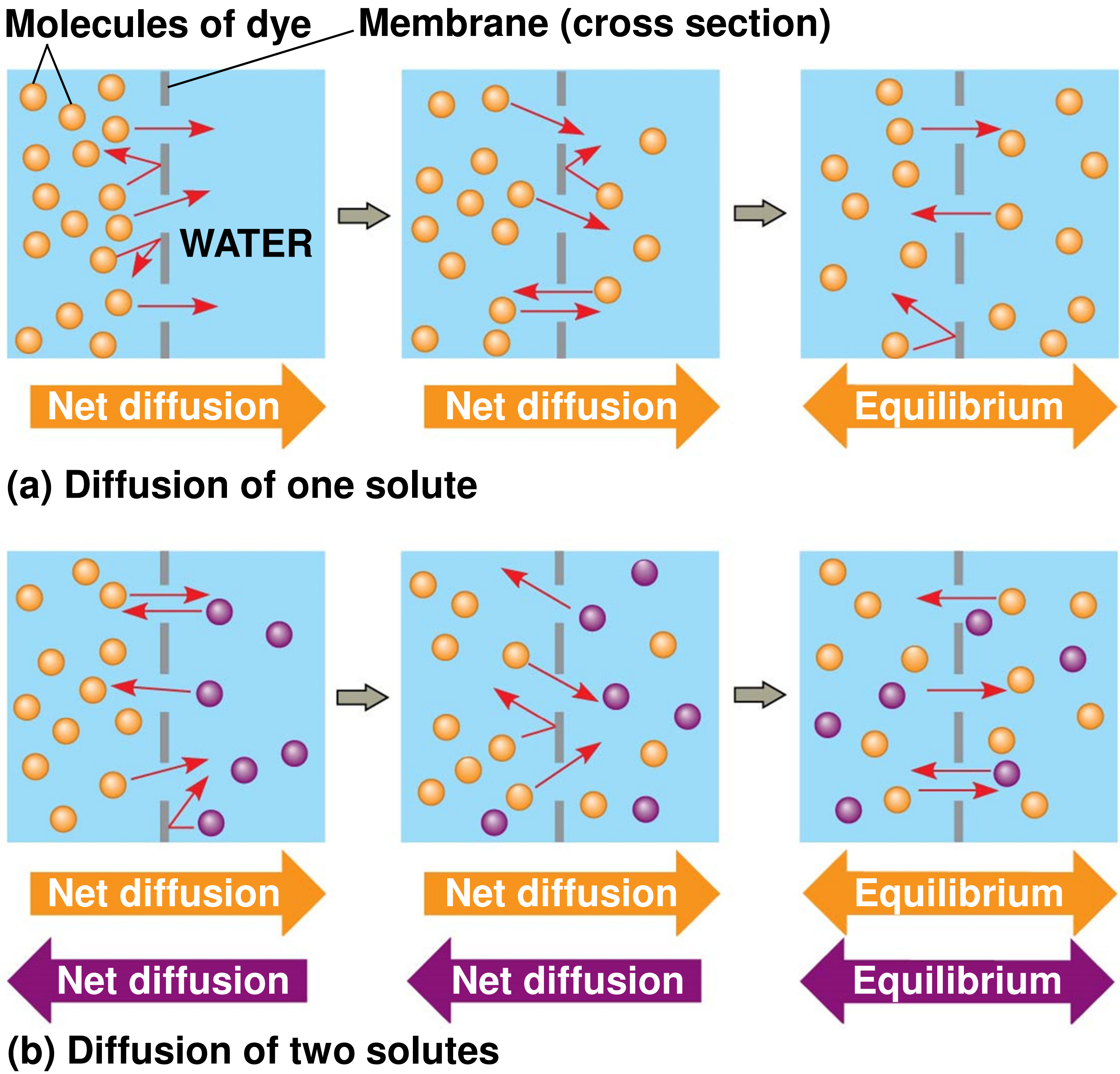
- **Diffusion** is the tendency for molecules to spread out evenly into the available space
- Although each molecule moves randomly, diffusion of a population of molecules may be directional
    - Substance moves from high to low concentration
- At dynamic equilibrium, as many molecules cross the membrane in one direction as in the other



Animation: Diffusion

Right click slide / Select play

Figure 5.9

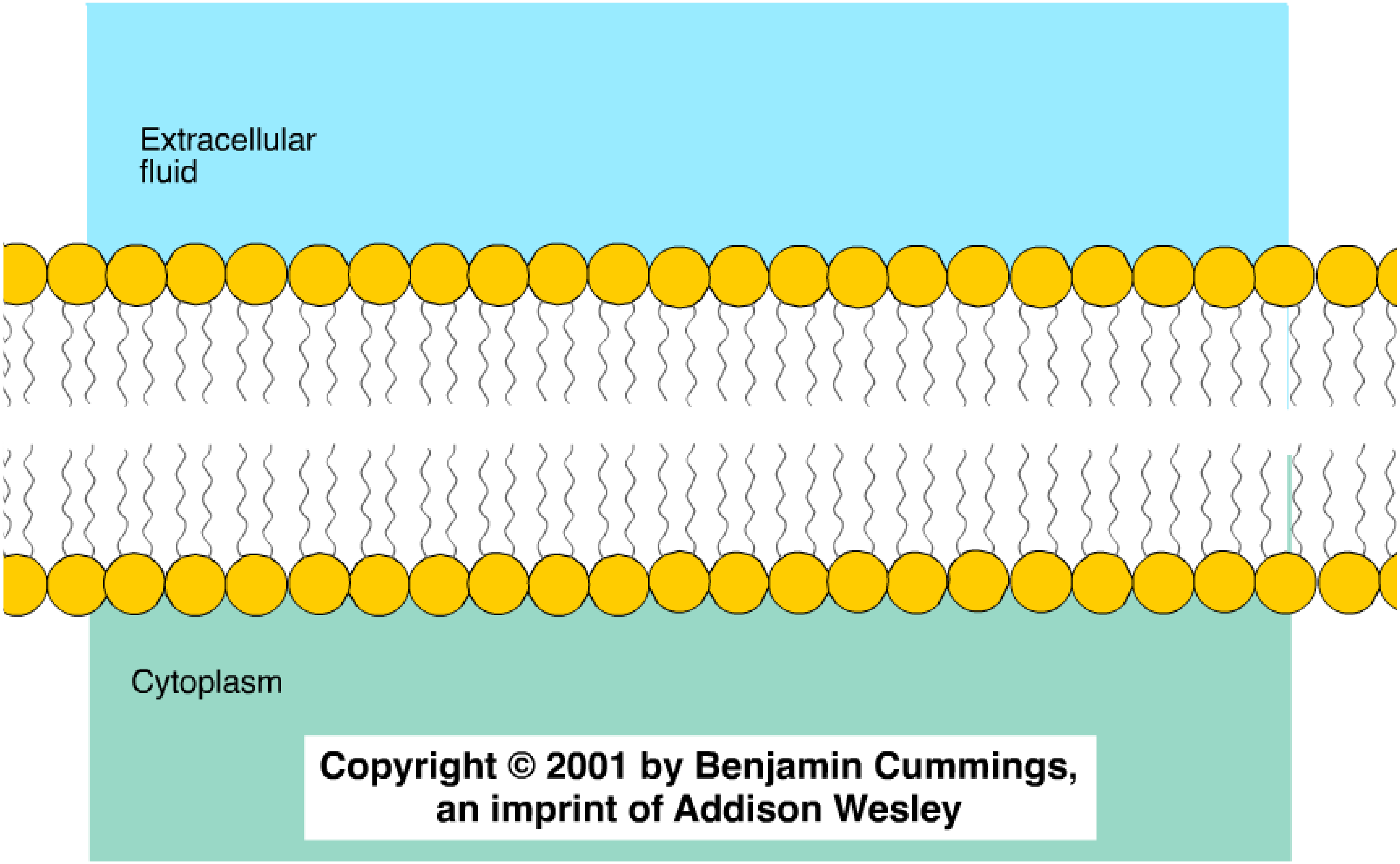


Molecules of dye
Membrane (cross section)
WATER
Net diffusion
Net diffusion
Equilibrium
(a) Diffusion of one solute
Net diffusion
Net diffusion
Equilibrium
Net diffusion
Net diffusion
Equilibrium
(b) Diffusion of two solutes

- Substances diffuse down their **concentration gradient**, from where it is more concentrated to where it is less concentrated
- The diffusion of a substance across a biological membrane is **passive transport** because no energy is expended by the cell to make it happen
  - No work must be done
  - Spontaneous
  - NO input of energy!

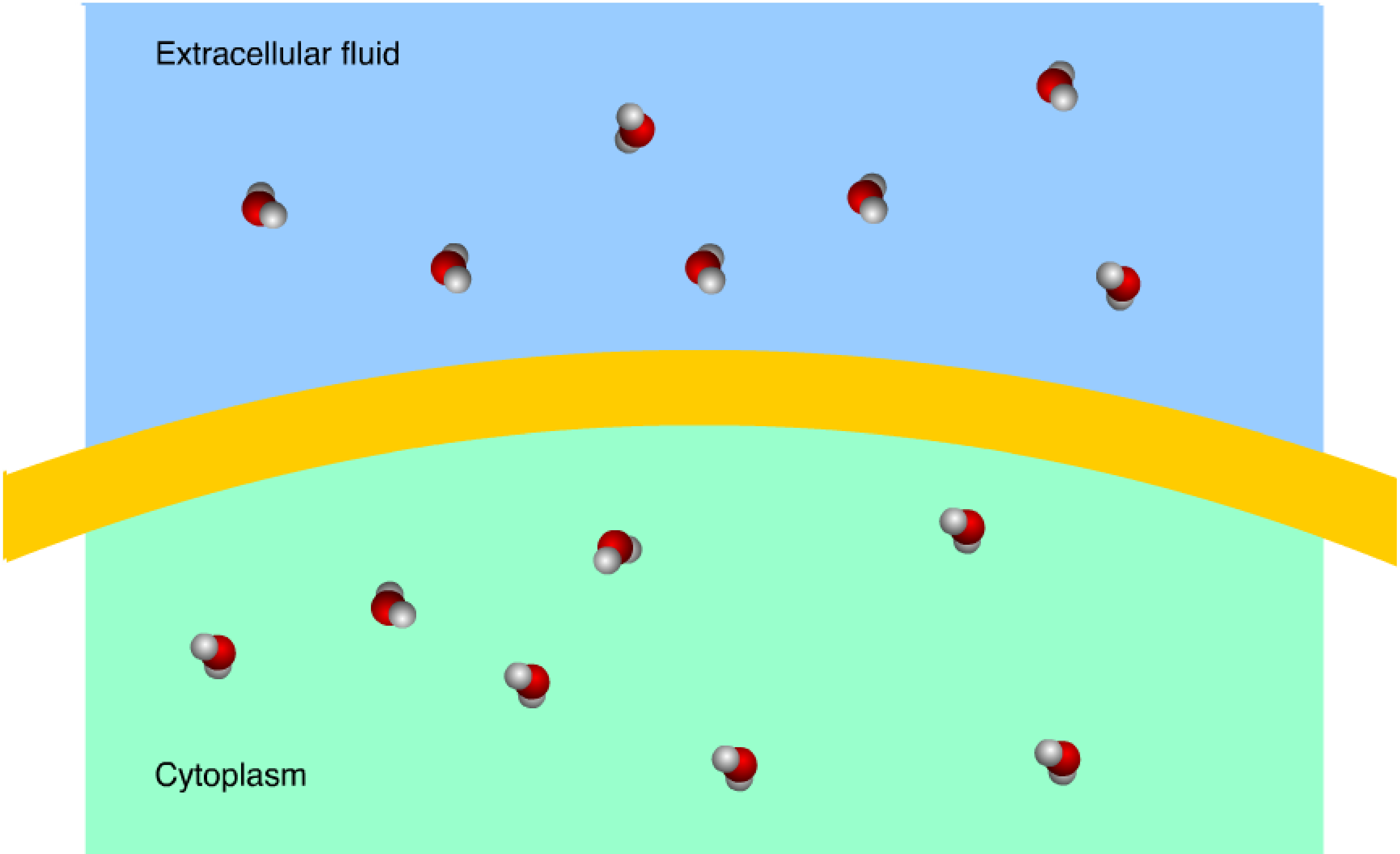
Effects of Osmosis on Water Balance

- **Osmosis** is the diffusion of free water across a selectively permeable membrane
- Water diffuses across a membrane until the solute concentration is equal on both sides
  - From the region of lower solute concentration
    - Which has a higher free water concentration
  - To the region of higher solute concentration
    - Which has a lower free water concentration



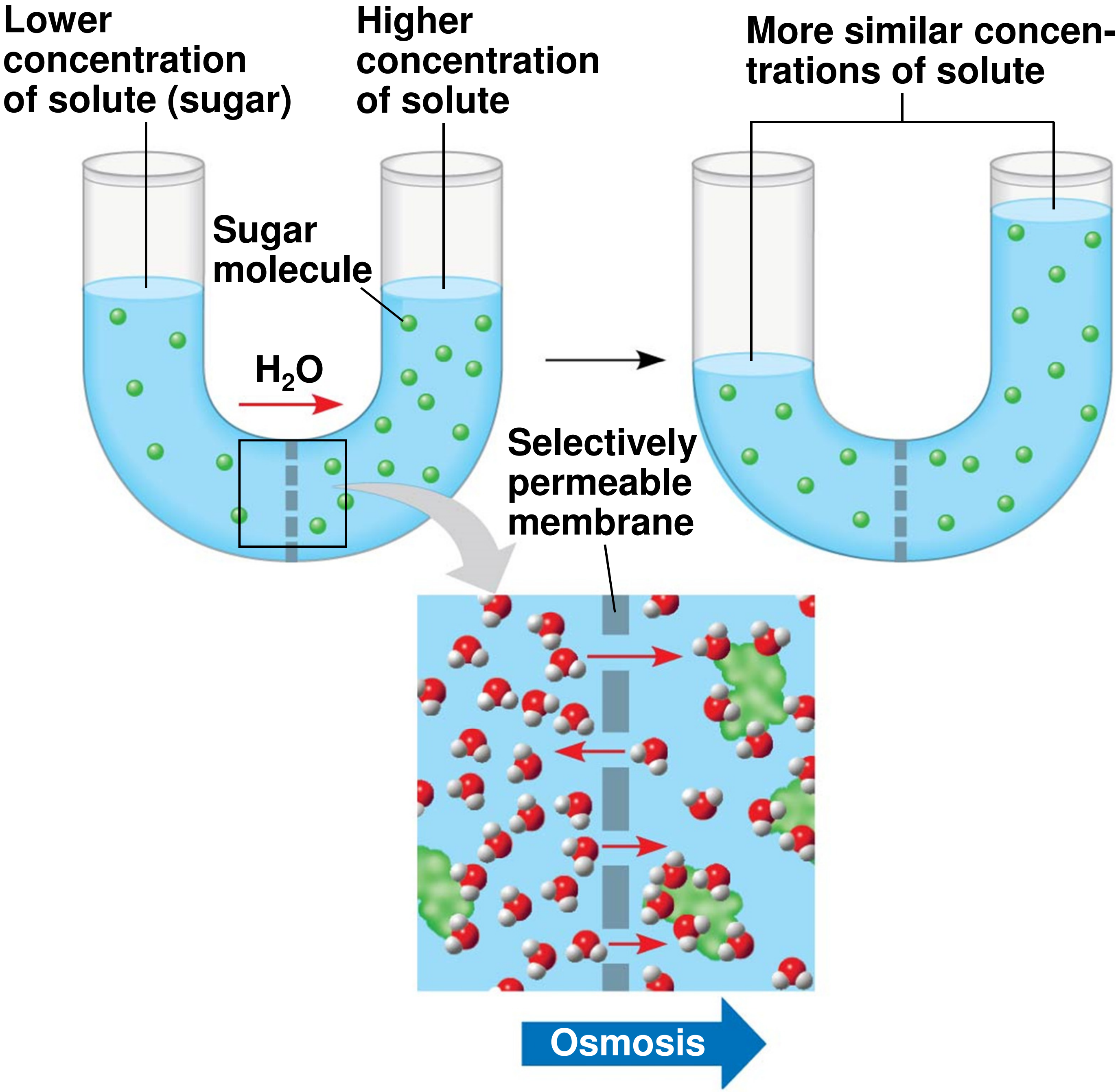
Animation: Membrane Selectivity

Right click slide / Select play



Animation: Osmosis
Right click slide / Select play

Figure 5.10



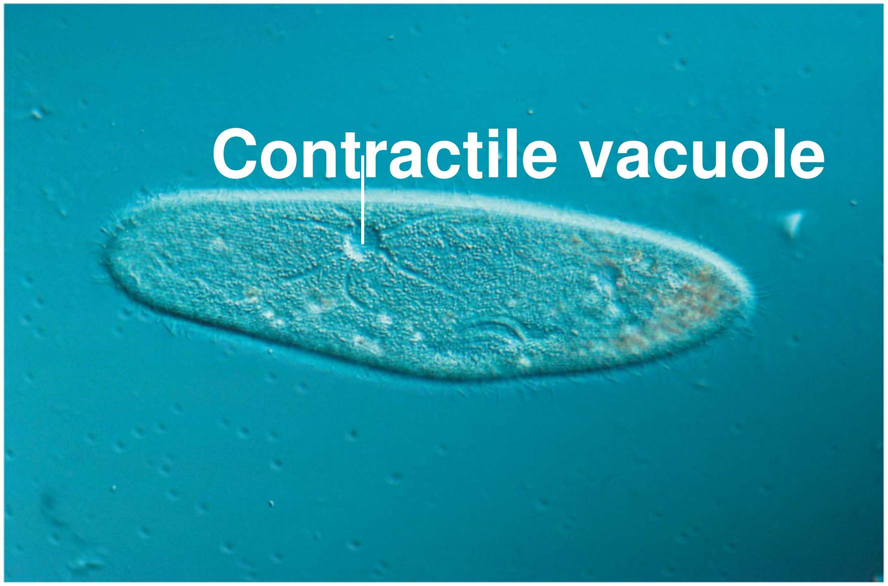
Lower concentration of solute (sugar)
Higher concentration of solute
More similar concen-trations of solute
Sugar molecule
H_2O
Selectively permeable membrane
Osmosis

Water Balance of Cells Without Walls

- Consider solute concentration AND membrane permeability to explain the behavior of a cell in a solution
- **Tonicity** is the ability of a surrounding solution to cause a cell to gain or lose water
- **Isotonic** solution
  - Solute concentration is the same as inside the cell
  - No net water movement across the plasma membrane

- **Hypertonic** solution
  - Solute concentration is greater than that inside the cell
  - Cell loses water
    - Animal cell: Crenation (cell shrivels/shrinks)
    - Plant cell: Plasmolysis (leads to plant death)
- **Hypotonic** solution
  - Solute concentration is less than that inside the cell
  - Cell gains water
    - Animal cell: Lysis (cell ruptures)
    - Plant cell: Turgid (normal)

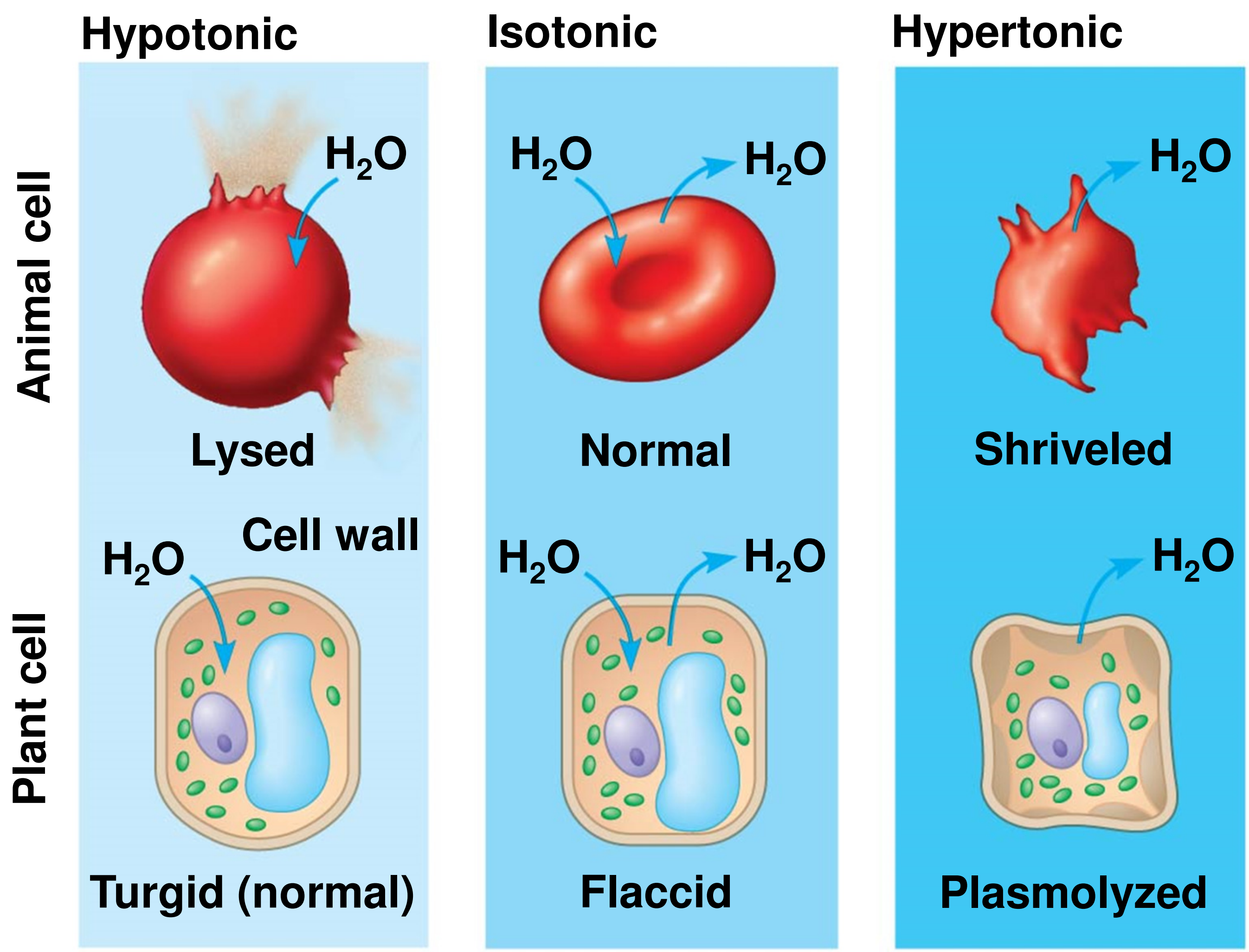
- Hypertonic or hypotonic environments create osmotic problems for organisms
- **Osmoregulation**, the control of solute concentrations and water balance, is a necessary adaptation for life in such environments
  - Some protists have a contractile vacuole that can pump excess water out of the cell



Water Balance of Cells with Walls

- Cell walls help maintain water balance
- A plant cell in a hypotonic solution swells until the wall exerts pressure back (called *turgor pressure*)
  - The cell is now **turgid** (very firm), which is the healthy state for most plants
- If a plant cell and its surroundings are isotonic, there is no net movement of water into the cell
  - The cell becomes **flaccid** (limp), and the plant may wilt
- In a hypertonic environment, plant cells lose water
  - Eventually the membrane pulls away from the wall, a usually lethal effect called **plasmolysis**

Figure 5.11



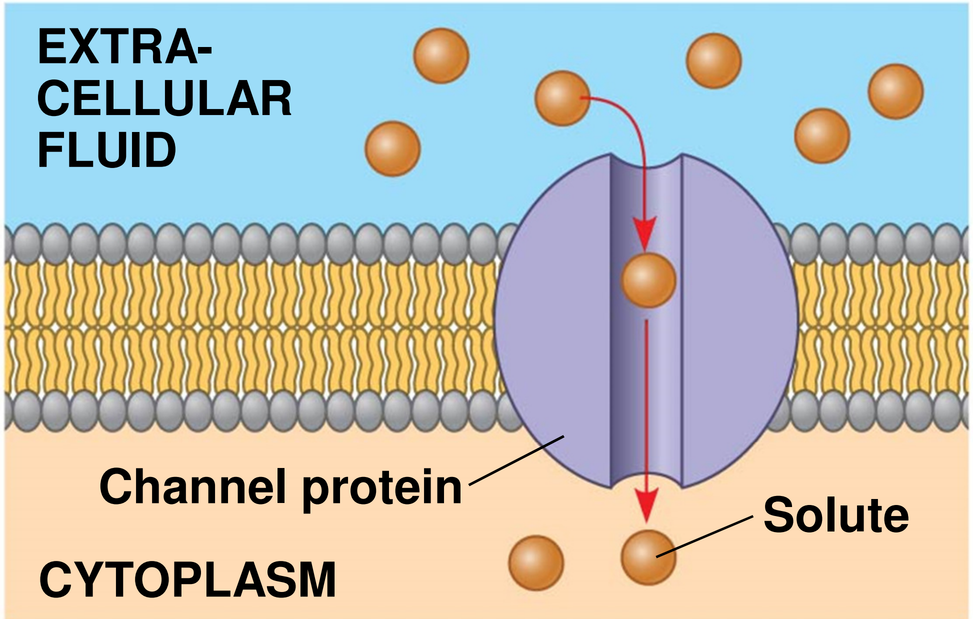
Hypotonic
Isotonic
Hypertonic
Animal cell
Plant cell
H_2O
H_2O
H_2O
H_2O
Lysed
Normal
Shriveled
Cell wall
H_2O
H_2O
H_2O
H_2O
Turgid (normal)
Flaccid
Plasmolyzed

Facilitated Diffusion: Passive Transport Aided by Proteins

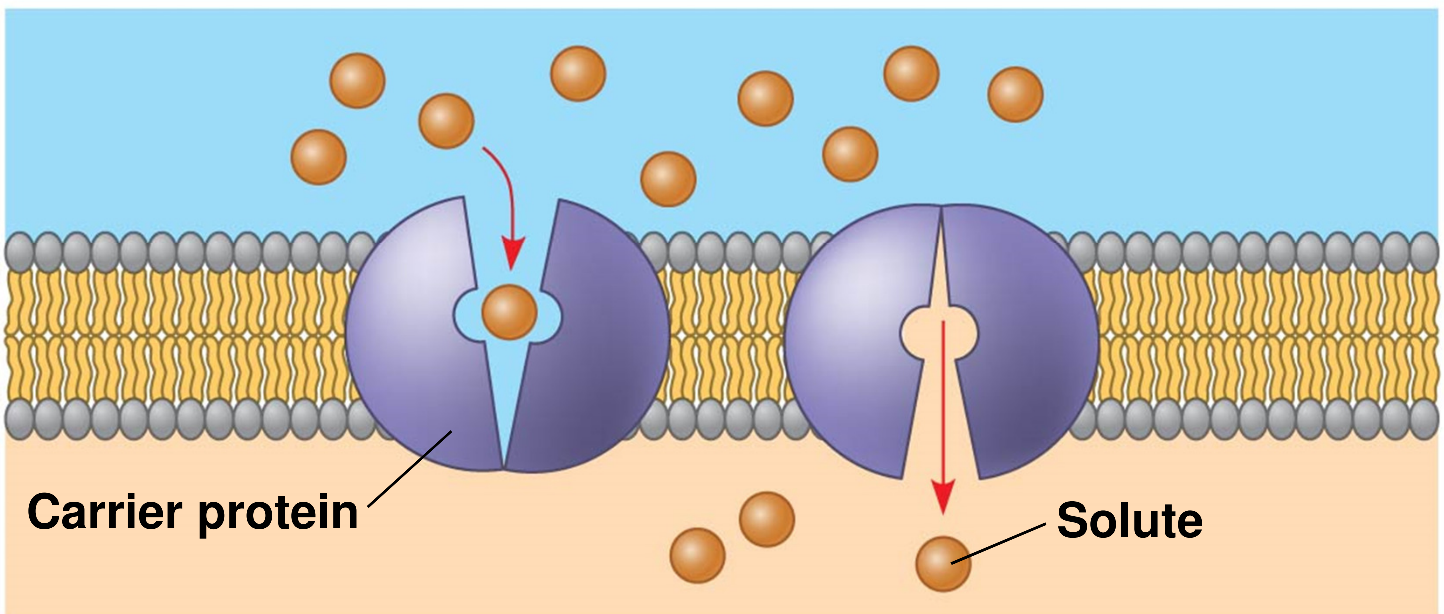
- In **facilitated diffusion**, transport proteins speed the passive movement of molecules across the plasma membrane
  - Still high to low but with the help of a protein
  - No energy input needed
- Transport proteins are very <u>specific</u>!
  - They transport some substances but not others

- Channel proteins provide corridors that allow a specific molecule or ion to cross the membrane
- Channel proteins include
  - Aquaporins, for facilitated diffusion of water
  - **Ion channels** that open or close in response to a stimulus (**gated channels**)
    - Important in nervous system
- Carrier proteins undergo a subtle change in shape that translocates the solute-binding site across the membrane
  - The shape change may be triggered by binding and release of the transported molecule

Figure 5.13



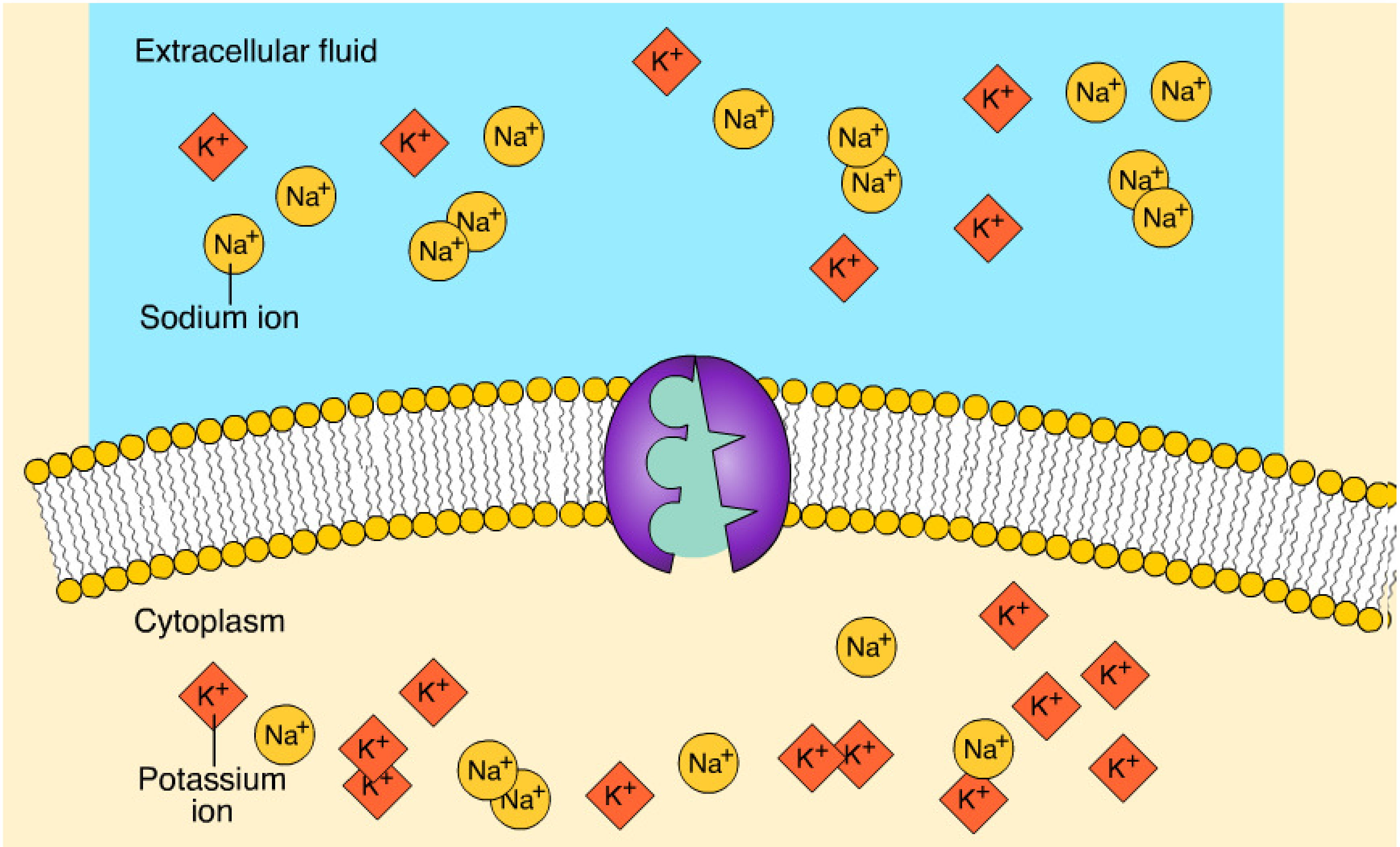
(a) A channel protein



(b) A carrier protein

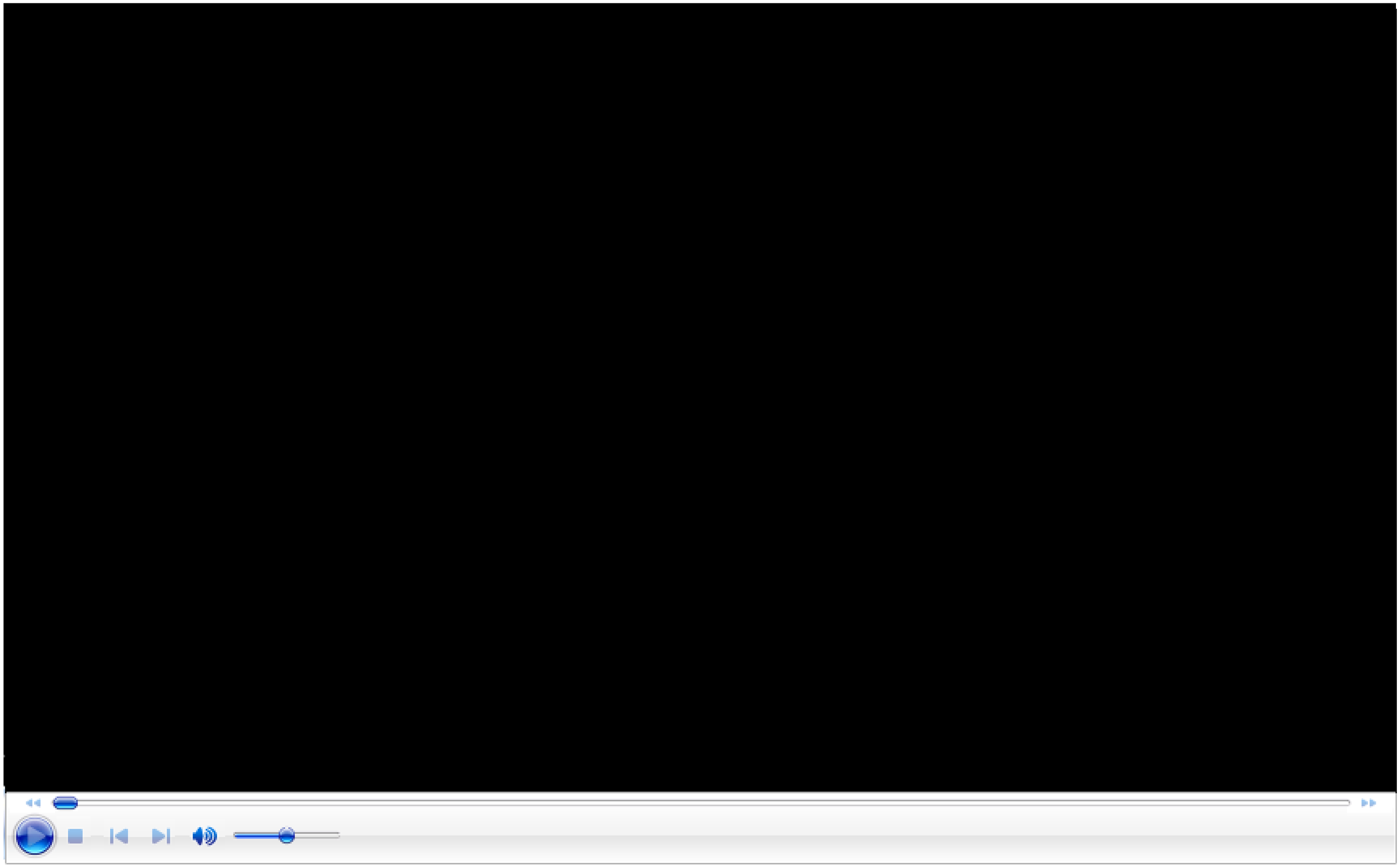
CONCEPT 5.4: Active transport uses energy to move solutes against their gradients

- **Active transport** moves substances *against* their concentration gradients
  - Requires *energy*, usually in the form of ATP
  - Allows cells to maintain concentration gradients that differ from their surroundings
- The **sodium-potassium pump** is one type of active transport system that maintains
  - Higher concentration of potassium ions (K+) inside cell
  - Lower concentration of sodium ions (Na+) inside cell
    - 3 Na+ ions are moved out of cell for every 2 K+ pumped into cell

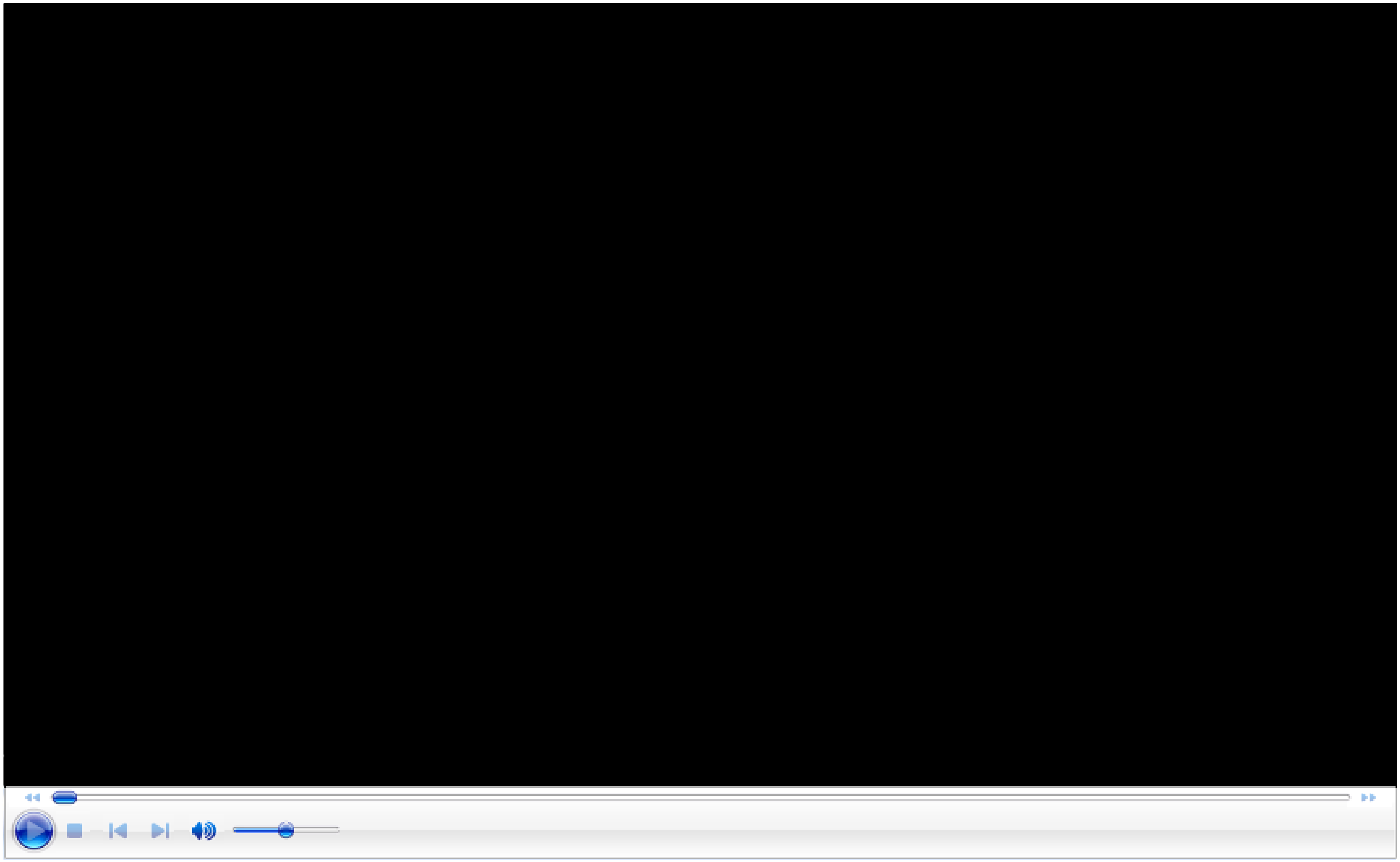


Animation: Active Transport

Right click slide / Select play

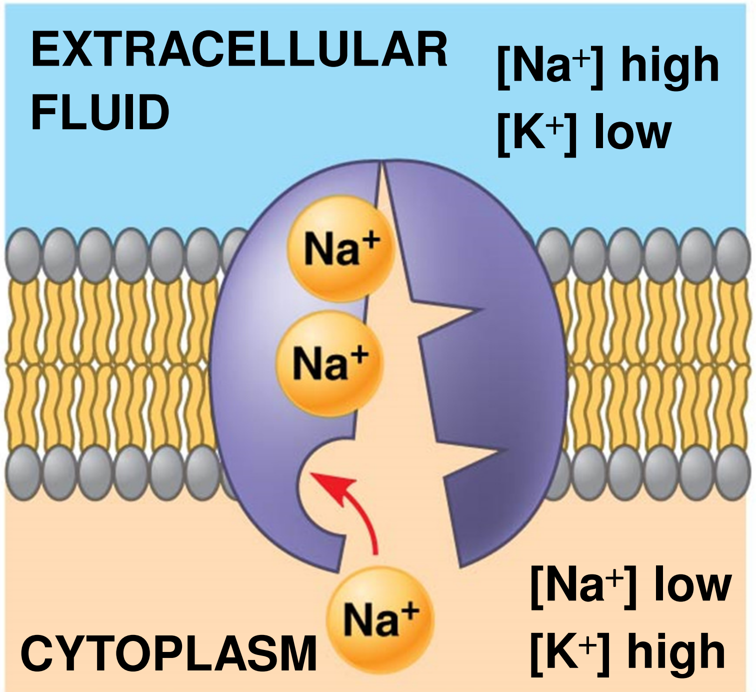


Video: Sodium-Potassium Pump

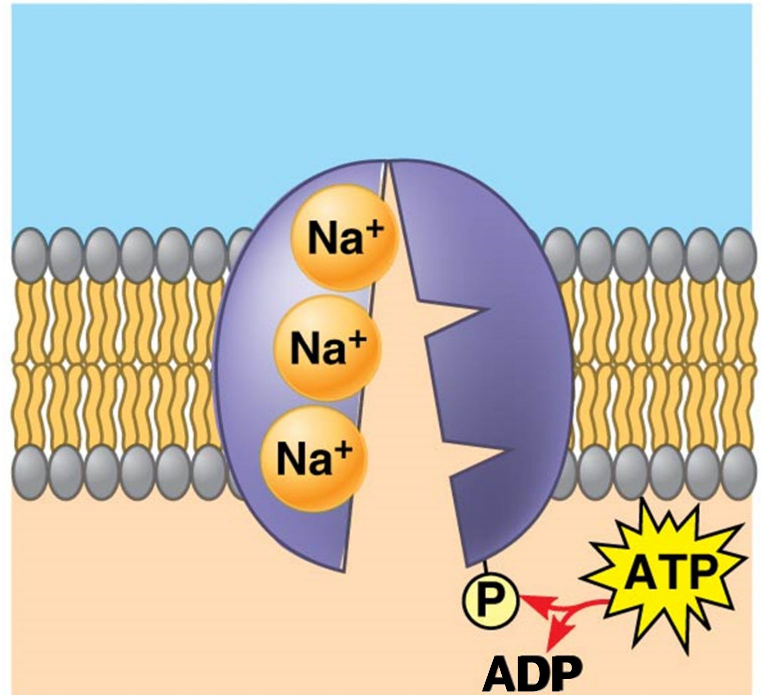


Video: Membrane Transport

Figure 5.14a

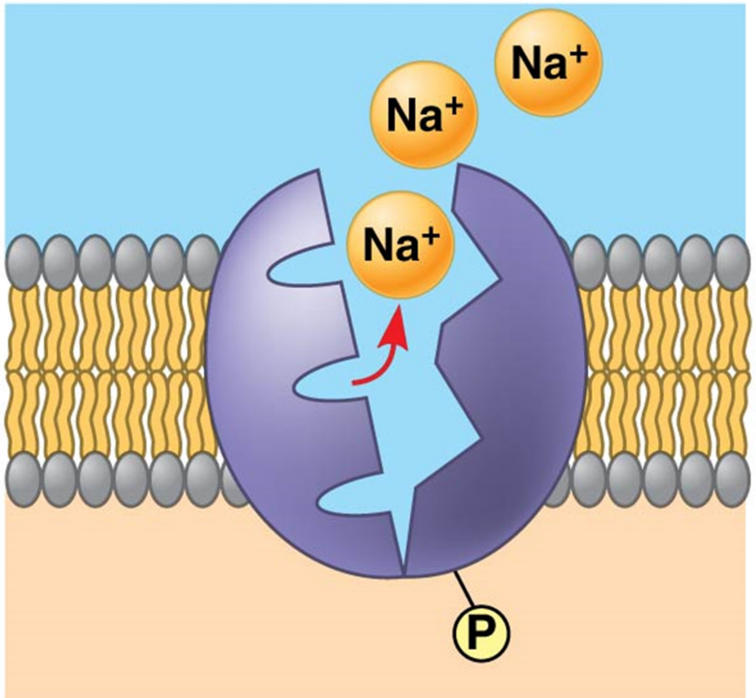


1 Cytoplasmic Na^+ binds to the sodium-potassium pump. The affinity for Na^+ is high when the protein has this shape.

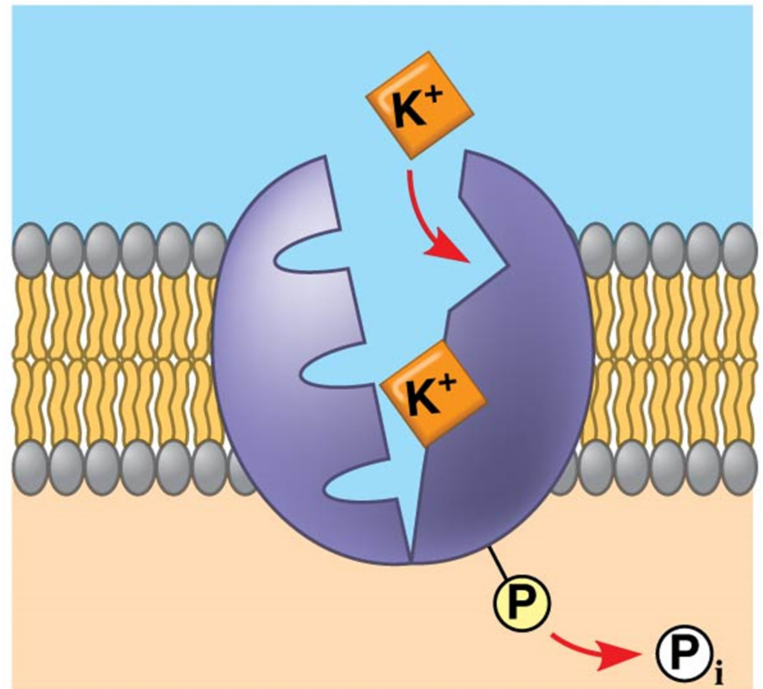


2 Na^+ binding stimulates phosphorylation by ATP.

Figure 5.14b

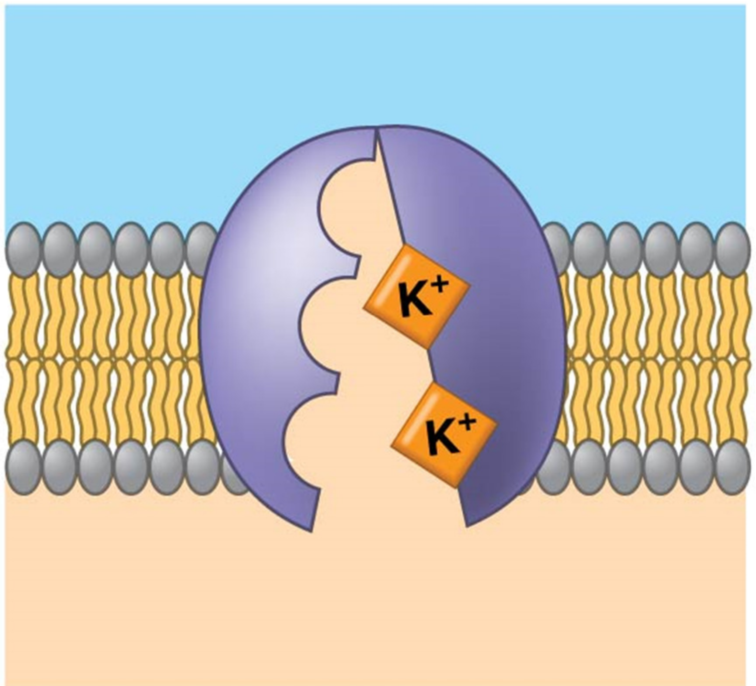


3 Phosphorylation leads to a change in protein shape, reducing its affinity for Na^+, which is released outside.

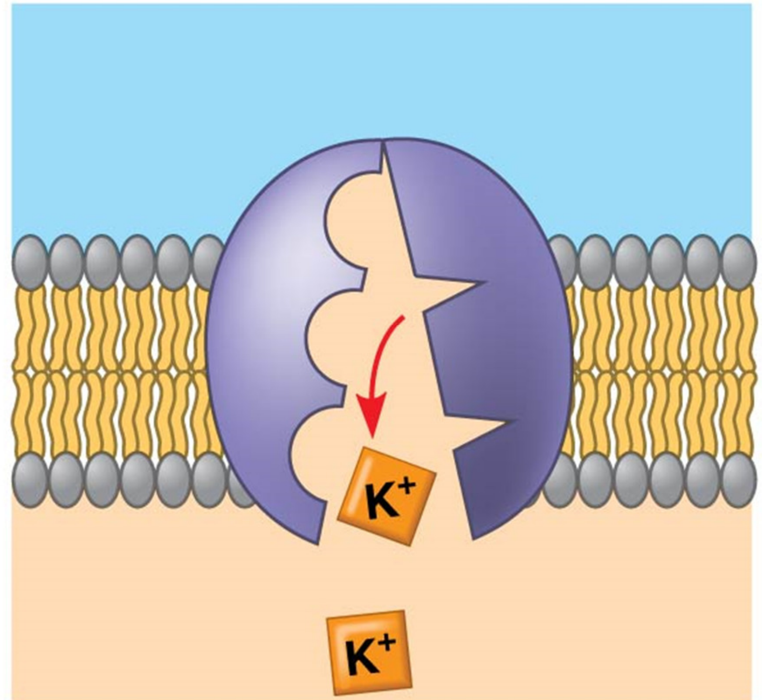


4 The new shape has a high affinity for K^+, which binds on the extracellular side and triggers release of the phosphate group.

Figure 5.14c

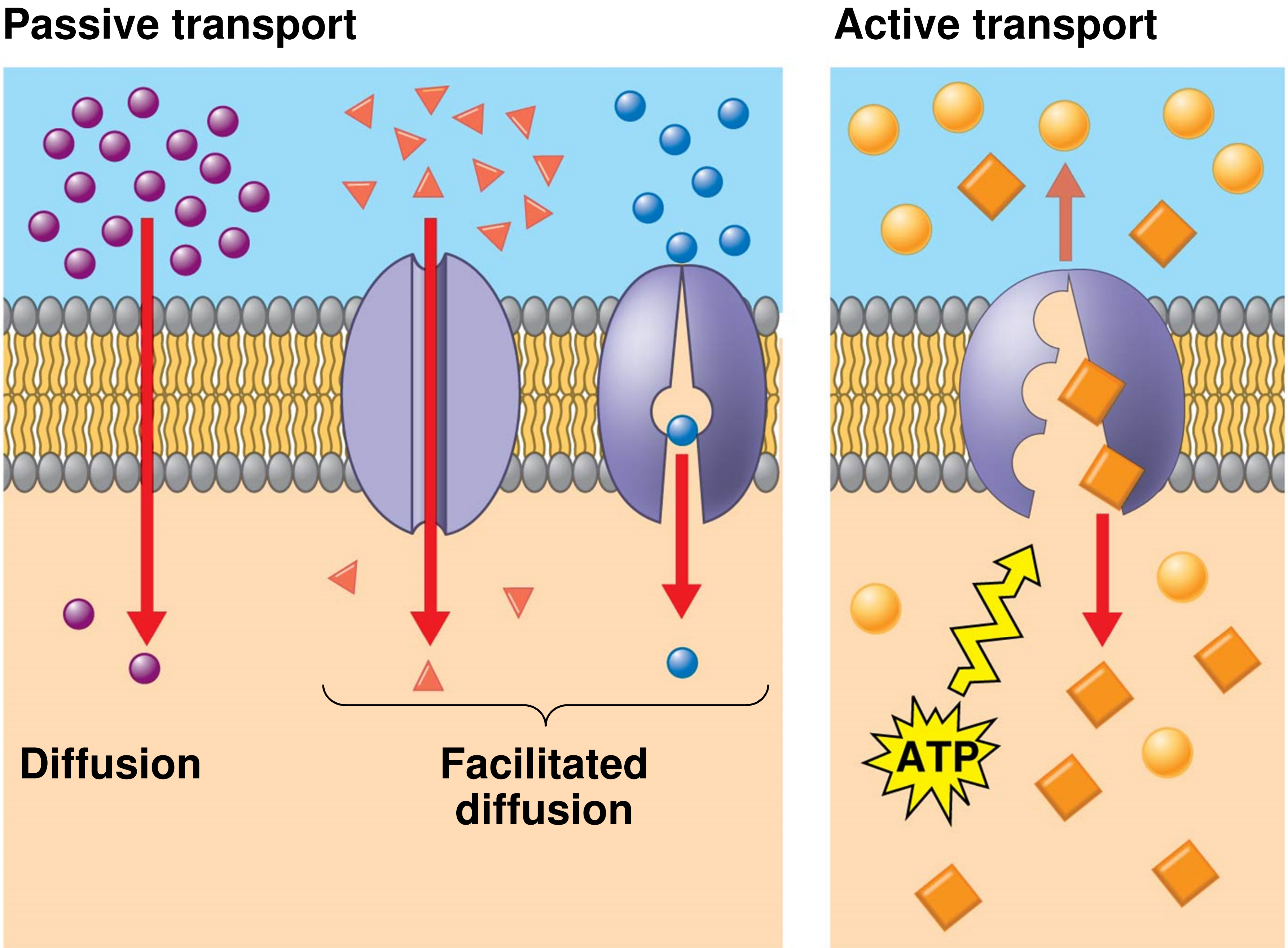


5 Loss of the phosphate group restores the protein's original shape, which has a lower affinity for K^+.



6 K^+ is released; affinity for Na^+ is high again, and the cycle repeats.

Figure 5.15


Passive transport
Active transport
ATP
Diffusion
Facilitated diffusion

How Ion Pumps Maintain Membrane Potential

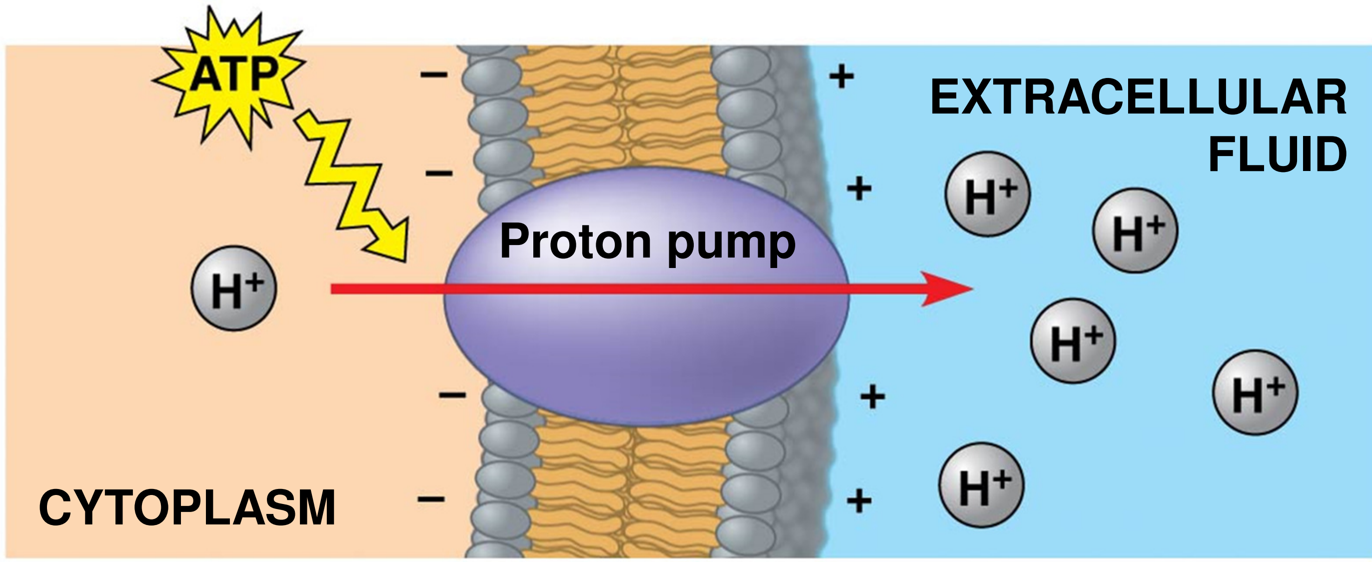
- **Membrane potential** is the voltage across a membrane
- Voltage is created by differences in the distribution of positive and negative ions across a membrane
    - Cytoplasmic side of the membrane (inside) is negative in charge relative to extracellular side (outside)
    - Membrane potential favors passive transport of cations into the cell and anions out of the cell

- Two combined forces, collectively called the **electrochemical gradient**, drive the diffusion of ions across a membrane
  - A chemical force (the ion's concentration gradient)
  - An electrical force (the effect of the membrane potential on the ion's movement)

- Electrochemical gradients and membrane potentials are important in the transmission of nerve impulses

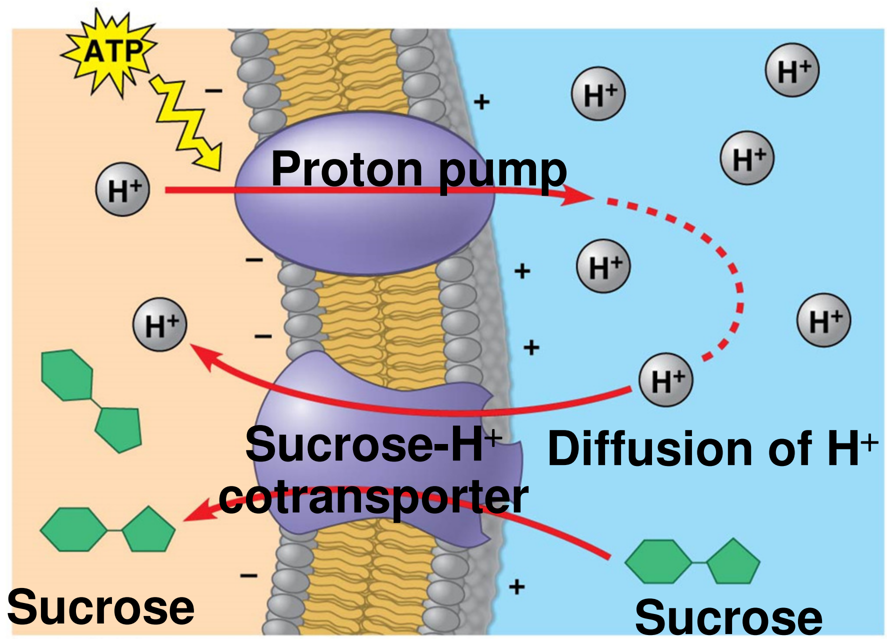
- An **electrogenic pump** is a transport protein that generates voltage across a membrane
  - The sodium-potassium pump is the major electrogenic pump of animal cells
  - The main electrogenic pump of plants, fungi, and bacteria is a **proton pump**
    - Actively transports protons (hydrogen ions, $H+$) out of the cell
- Electrogenic pumps help store energy that can be used for cellular work

Figure 5.16



Cotransport: Coupled Transport by a Membrane Protein

- **Cotransport** occurs when active transport of a solute indirectly drives transport of other solutes
  - A substance that has been pumped across a membrane can do work as it moves back across membrane by diffusion



CONCEPT 5.5: Bulk transport across the plasma membrane occurs by exocytosis and endocytosis

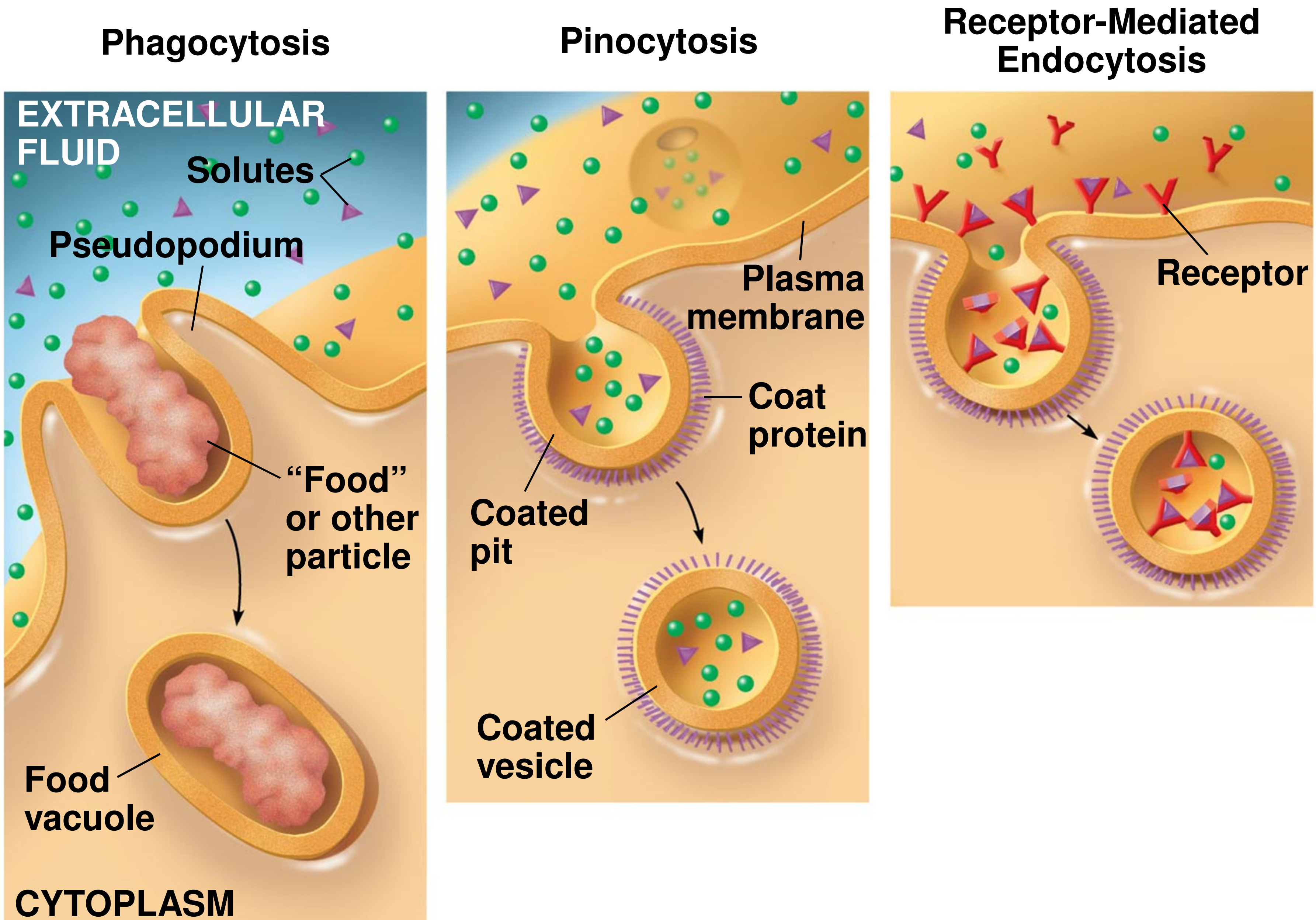
- Small solutes and water enter or leave the cell through the lipid bilayer or by means of transport proteins
- Large molecules, such as polysaccharides and proteins, cross the membrane in bulk by means of vesicles
  - Bulk transport requires energy

Exocytosis and Endocytosis

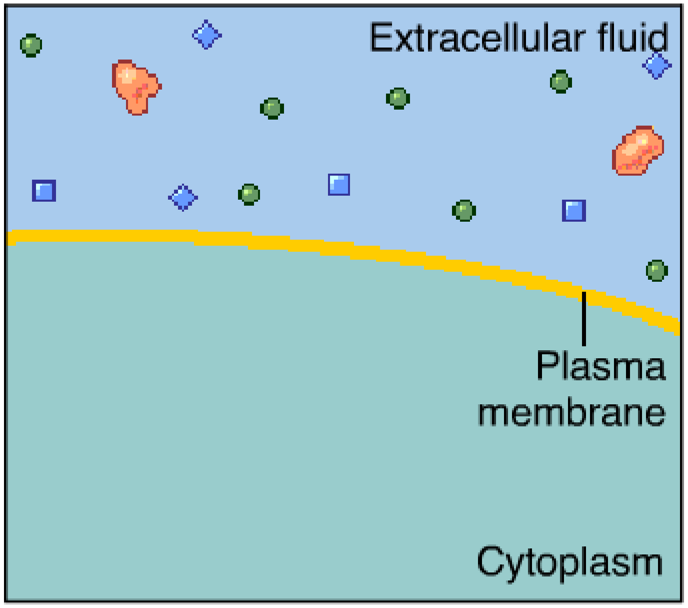
- In **exocytosis**, transport vesicles migrate to the membrane, fuse with it, and release their contents
  - EXIT
  - Many secretory cells use exocytosis to export products (like insulin or neurotransmitters)
- In **endocytosis**, the cell takes in molecules and particulate matter by forming new vesicles from the plasma membrane
  - IN

- Endocytosis is a reversal of exocytosis, involving different proteins
- There are three types of endocytosis
  - **Phagocytosis**
    - "Cellular eating"
  - **Pinocytosis**
    - "Cellular drinking"
  - **Receptor-mediated endocytosis**
    - Specialized type of endocytosis that enables cells to acquire bulk quantities of specific substances

Figure 5.18



Phagocytosis
Pinocytosis
Receptor-Mediated
Endocytosis
EXTRACELLULAR
FLUID
Solutes
Pseudopodium
"Food"
or other
particle
Food
vacuole
CYTOPLASM
Plasma
membrane
Coat
protein
Coated
pit
Coated
vesicle
Receptor



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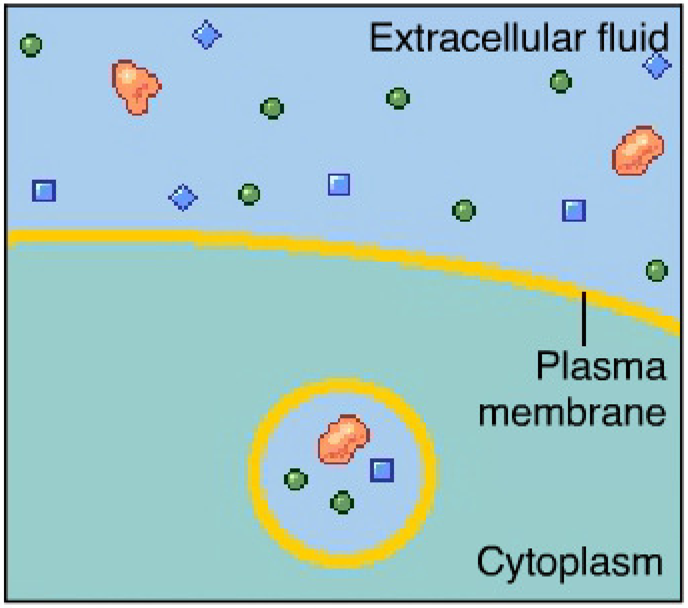
Animation: Exocytosis Endocytosis Introduction
Right click slide / Select play



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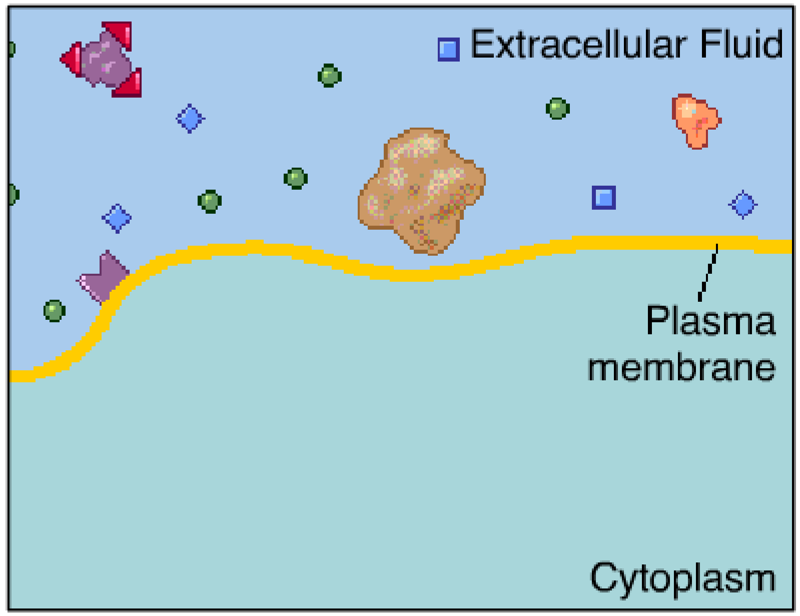
Animation: Exocytosis
Right click slide / Select play



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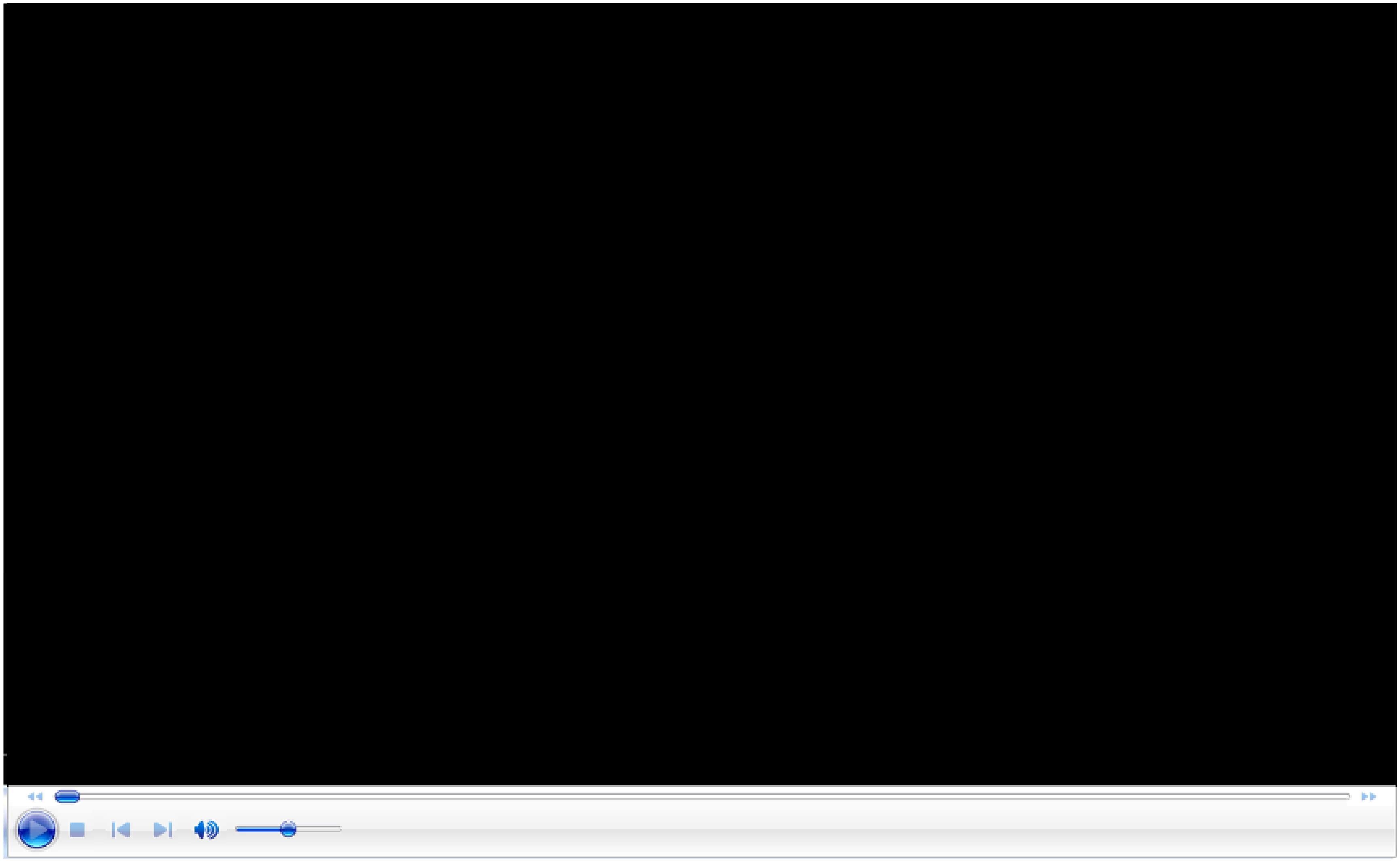
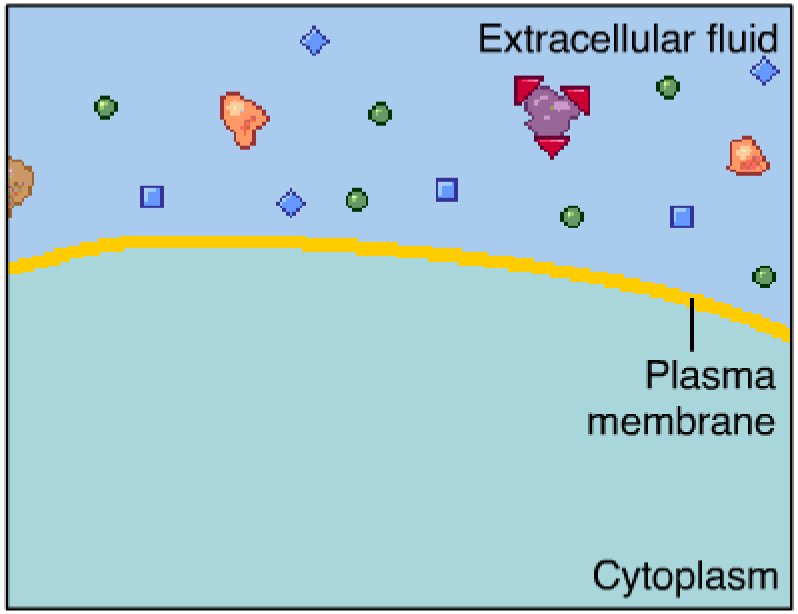
Animation: Phagocytosis

Right click slide / Select play



Video: Phagocytosis



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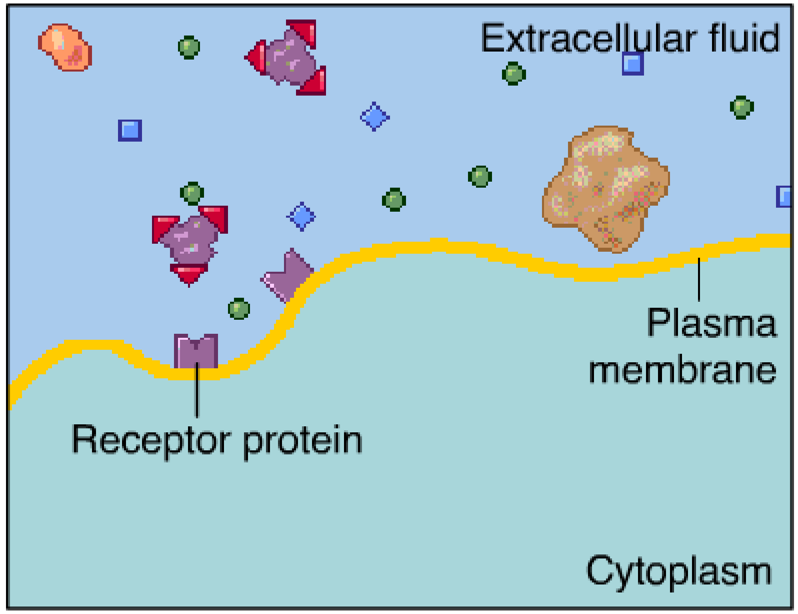
Animation: Pinocytosis

Right click slide / Select play



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Animation: Receptor-Mediated Endocytosis
Right click slide / Select play

CONCEPT 5.6: The plasma membrane plays a key role in most cell signaling

- In multicellular organisms, cell-to-cell communication allows the cells of the body to coordinate their activities
- Communication between cells is also essential for many unicellular organisms

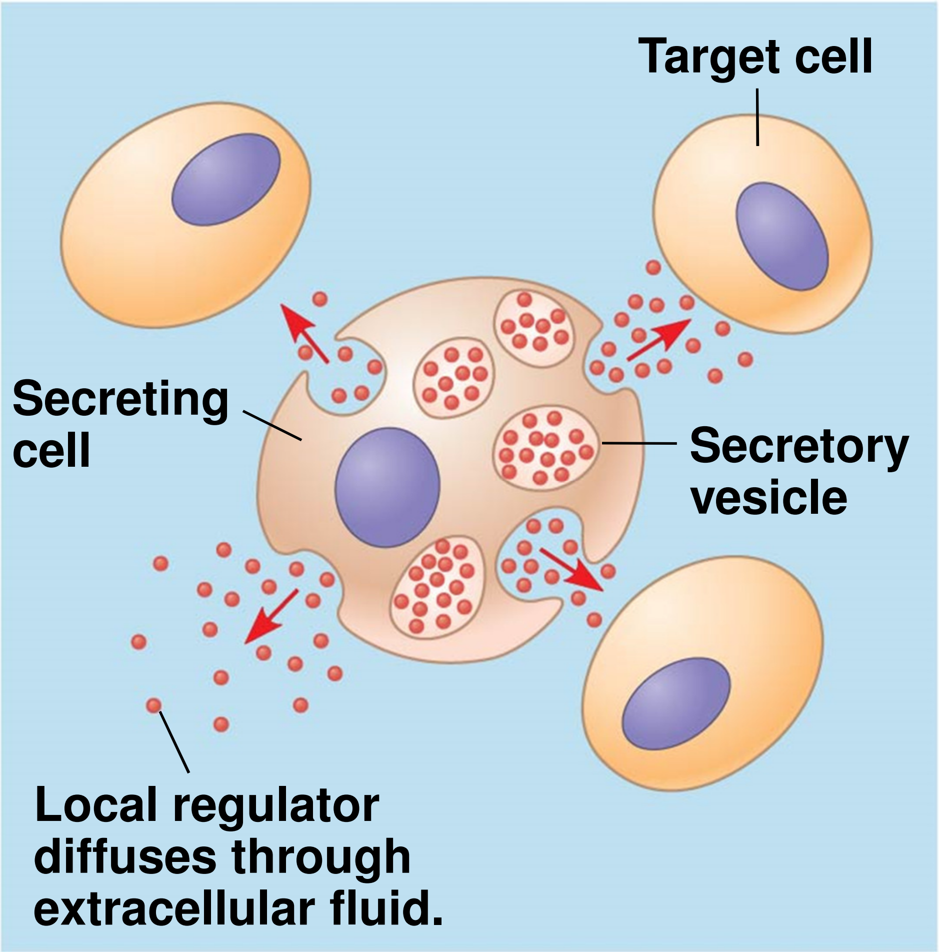
Local Signaling

- Eukaryotic cells may communicate by direct contact
- Animal and plant cells have junctions that directly connect the cytoplasm of adjacent cells
  - Animal cells-gap junctions
  - Plants cells-plasmodesmata
- The free passage of substances in the cytosol from one cell to another is a type of local signaling

- In many other cases of local signaling, messenger molecules are secreted by a signaling cell
- These messenger molecules, called **local regulators**, travel only <u>short distances</u>
  - One class of these, *growth factors*, stimulates nearby cells to grow and divide
    - This type of local signaling in animal cells is called *paracrine signaling*

Figure 5.19a

Local signaling

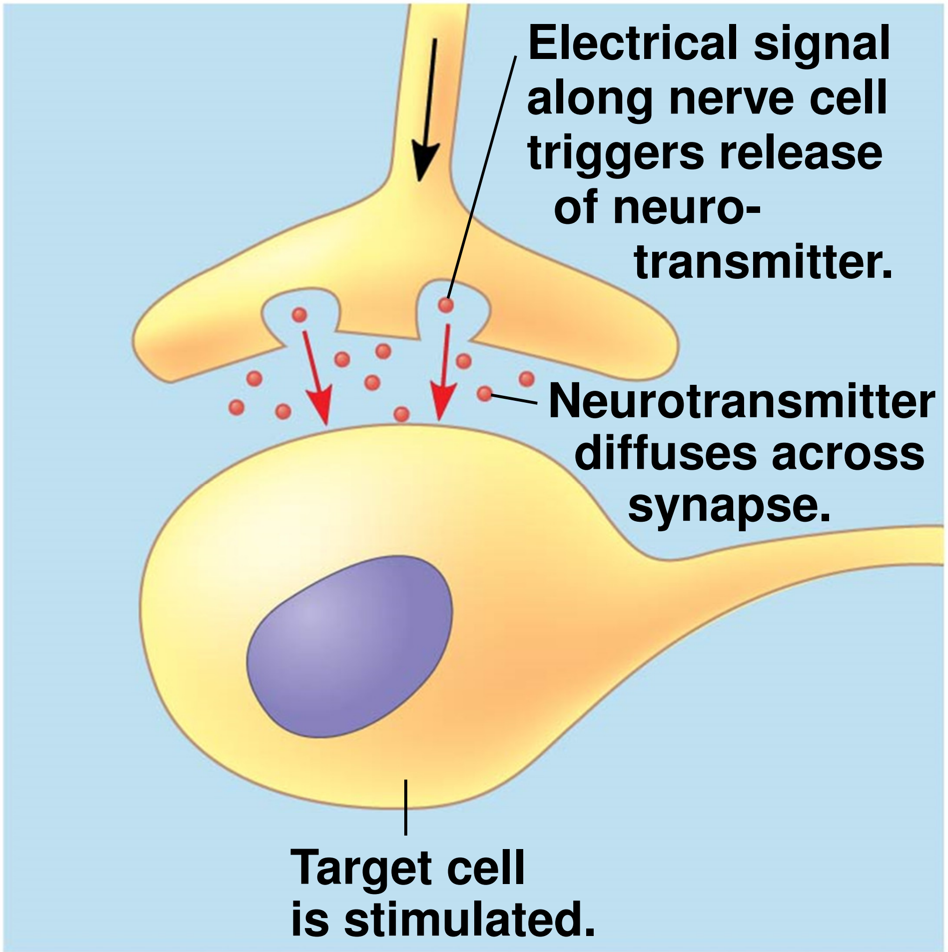


(a) Paracrine signaling

- Another more specialized type of local signaling occurs in the animal nervous system
- This *synaptic signaling* consists of an electrical signal moving along a nerve cell that triggers secretion of neurotransmitter molecules
- These diffuse across the space between the nerve cell and its target, triggering a response in the target cell

Figure 5.19b

Local signaling

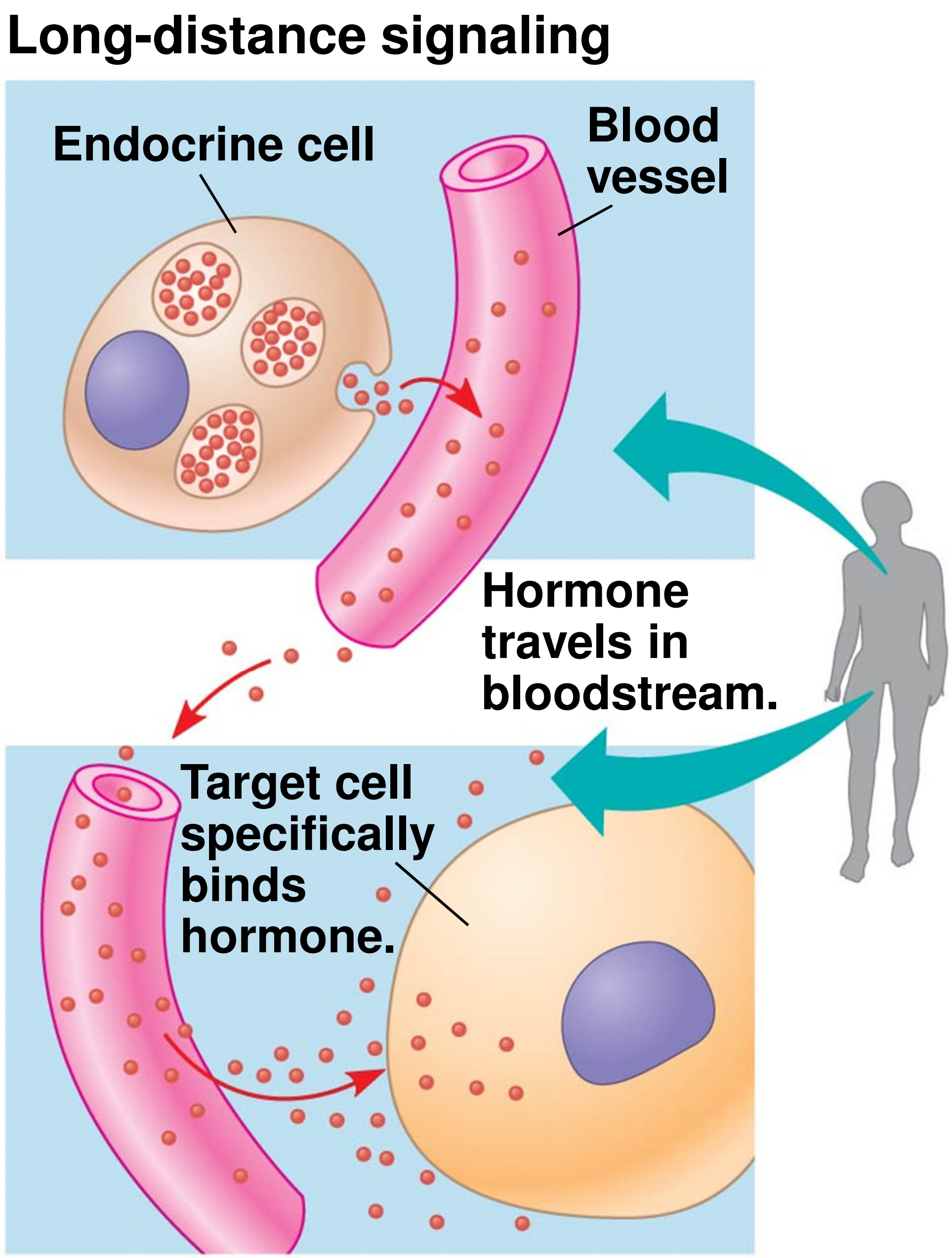


(b) Synaptic signaling

Long-Distance Signaling

- In long-distance signaling, plants and animals use chemicals called **hormones**
- In hormonal signaling in animals (called *endocrine signaling*), specialized cells release hormone molecules that travel via the circulatory system
- Hormones vary widely in size and shape
  - Ethylene-plant hormone
  - Insulin-mammalian hormone

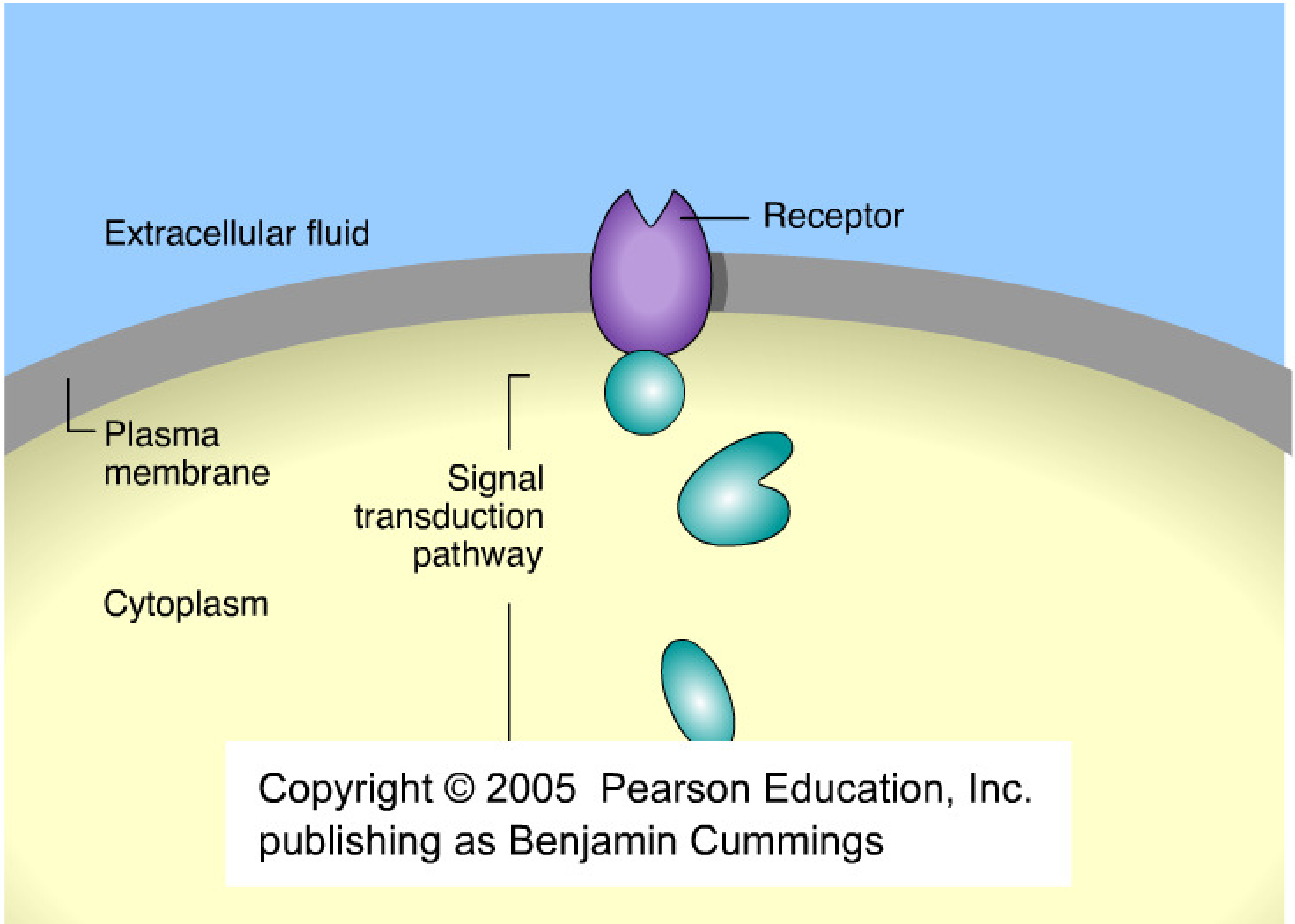
Figure 5.19c



(c) Endocrine (hormonal) signaling

The Three Stages of Cell Signaling: *A Preview*

- Earl W. Sutherland discovered how the hormone epinephrine acts on cells
- Sutherland suggested that cells receiving signals undergo three processes
  - **Reception**
    - Target cell's detection of a signaling molecule coming from outside the cell
  - **Transduction**
    - Steps that convert the signal to a form that can bring about a specific response
  - **Response**
    - Change in activity brought about by transduced signal



Animation: Signaling Overview
Right click slide / Select play

Figure 5.20-1

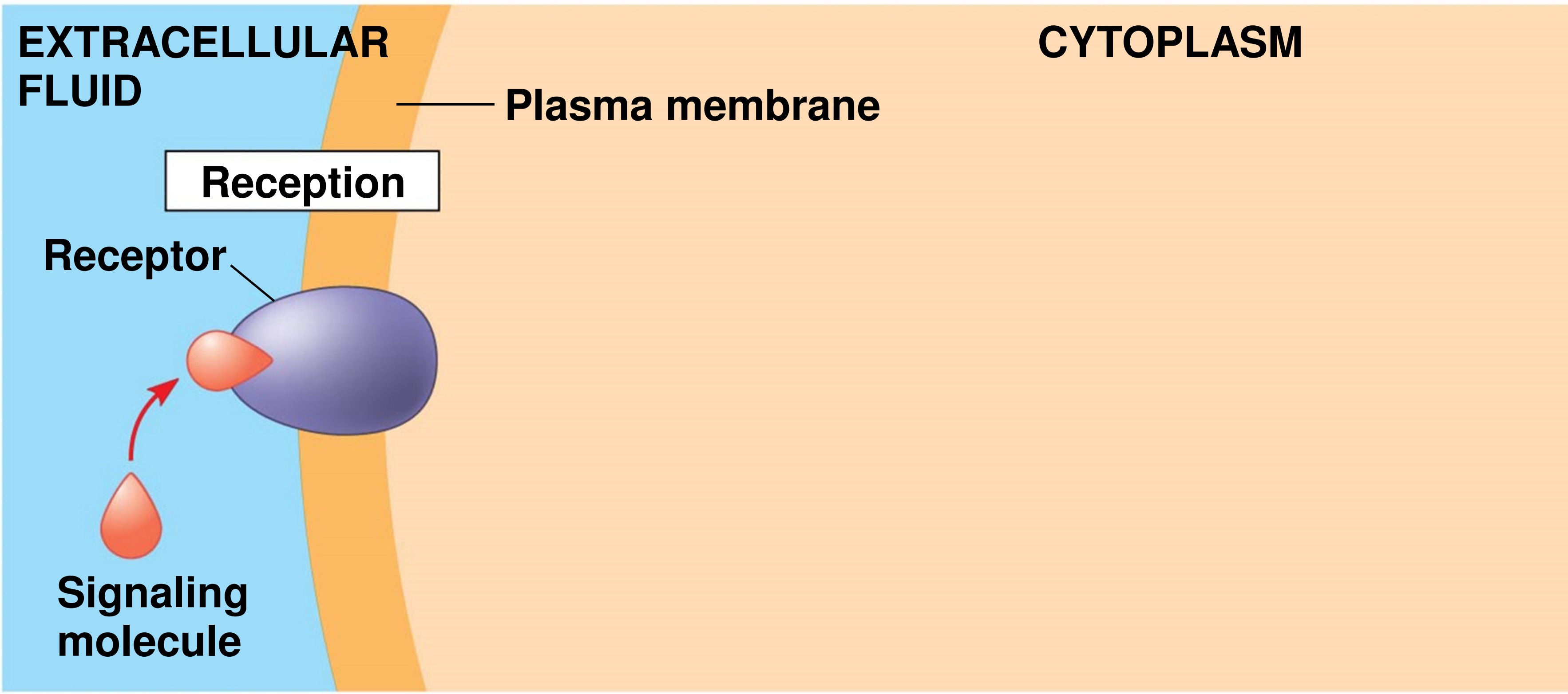
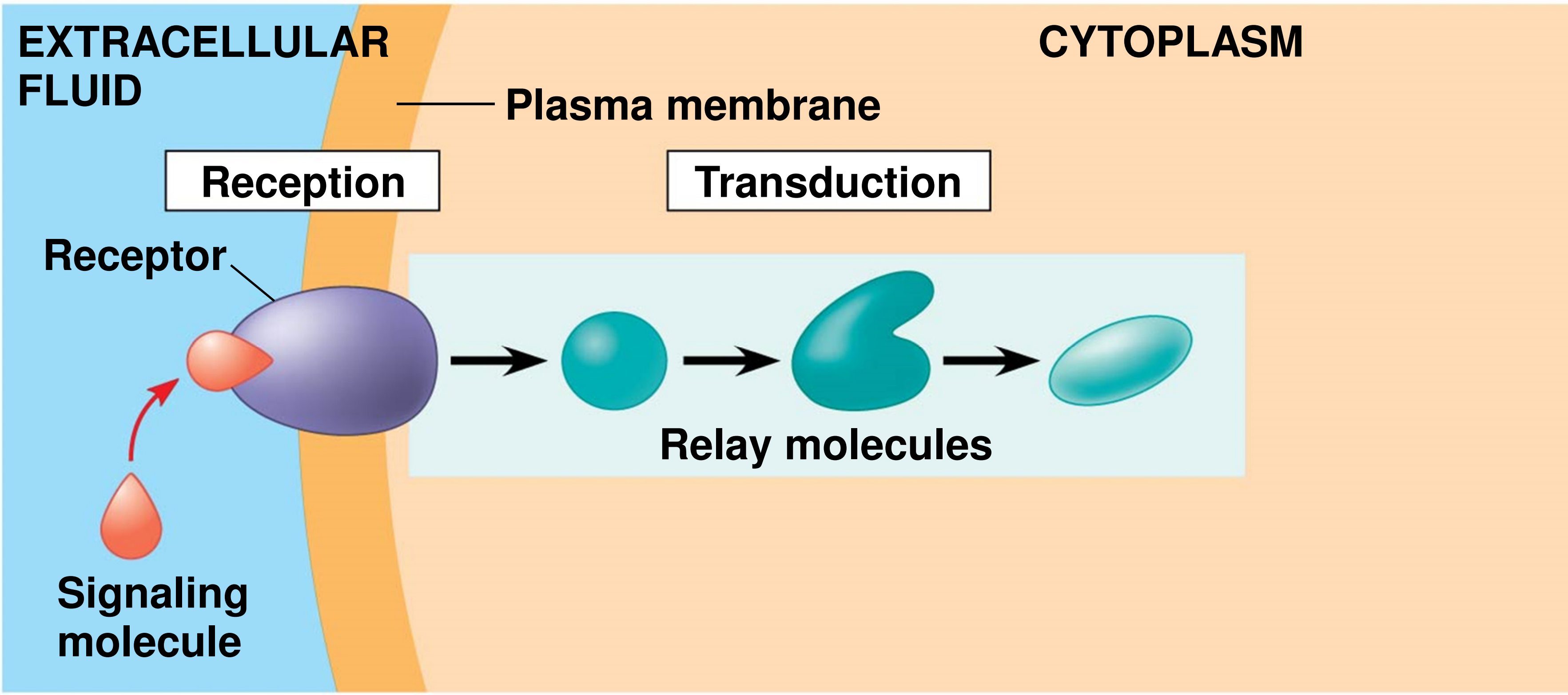
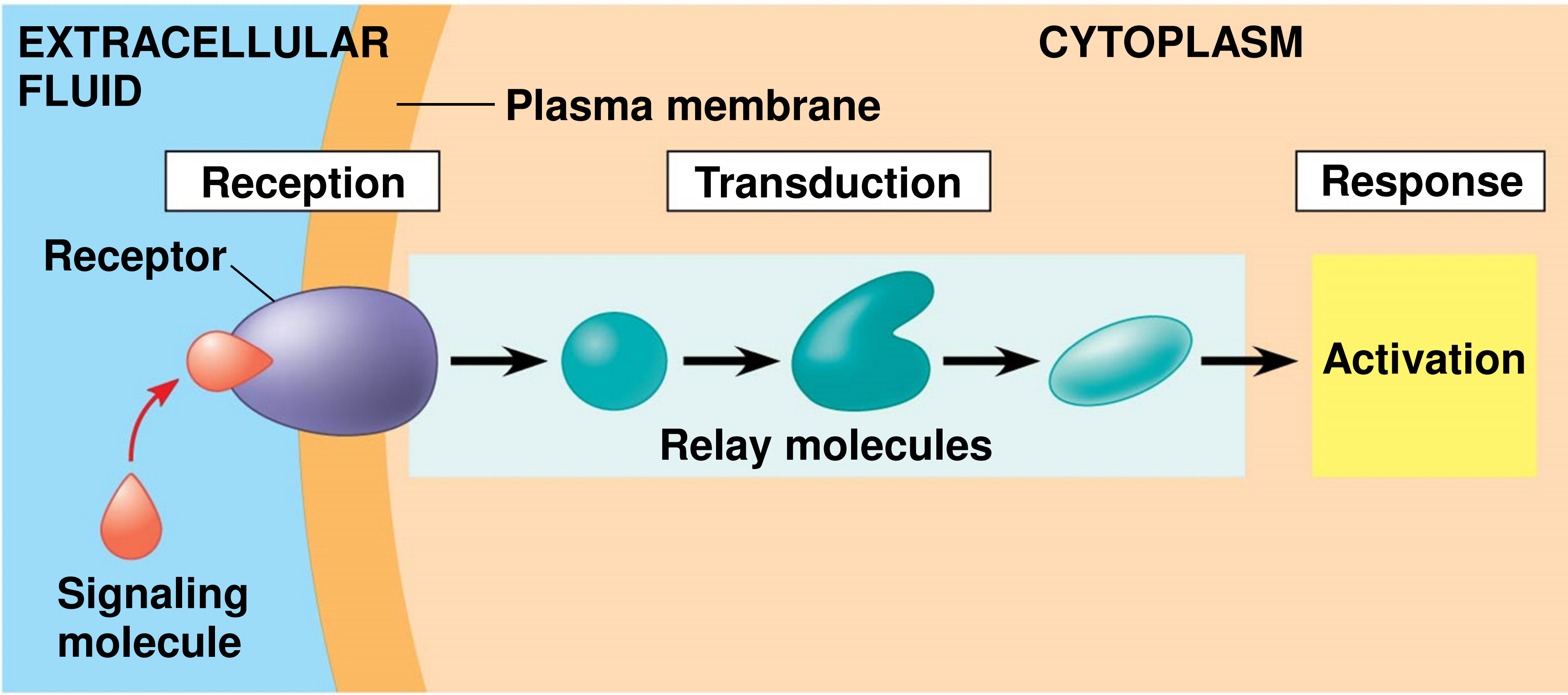

EXTRACELLULAR FLUID
CYTOPLASM
Plasma membrane
Reception
Receptor
Signaling molecule

Figure 5.20-2



EXTRACELLULAR FLUID
CYTOPLASM
Plasma membrane
Reception
Transduction
Receptor
Relay molecules
Signaling molecule

Figure 5.20-3



EXTRACELLULAR FLUID
CYTOPLASM
Plasma membrane
Reception
Transduction
Response
Receptor
Activation
Relay molecules
Signaling molecule

Reception, the Binding of a Signaling Molecule to a Receptor Protein

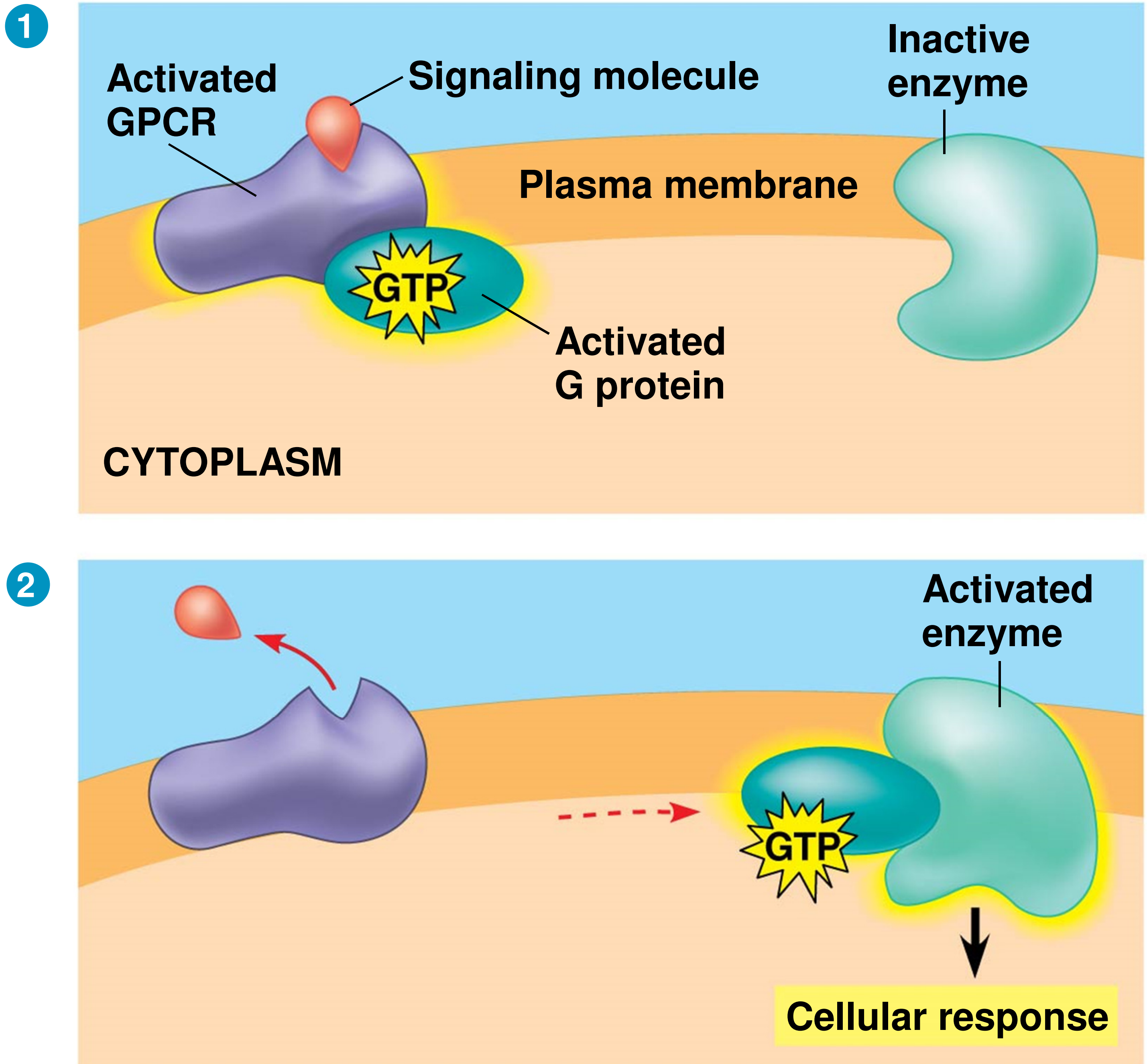
- The binding between a signal molecule (**ligand**) and receptor is highly specific
  - Complementary in SHAPE (lock and key)
- Ligand binding generally causes a shape change in the receptor
  - This activates the receptor
- Most signal receptors are plasma membrane proteins

Receptors in the Plasma Membrane

- Most water-soluble signal molecules bind to specific sites on receptor proteins that span the plasma membrane
- There are two main types of membrane receptors
  - G protein-coupled receptors
  - Ligand-gated ion channels

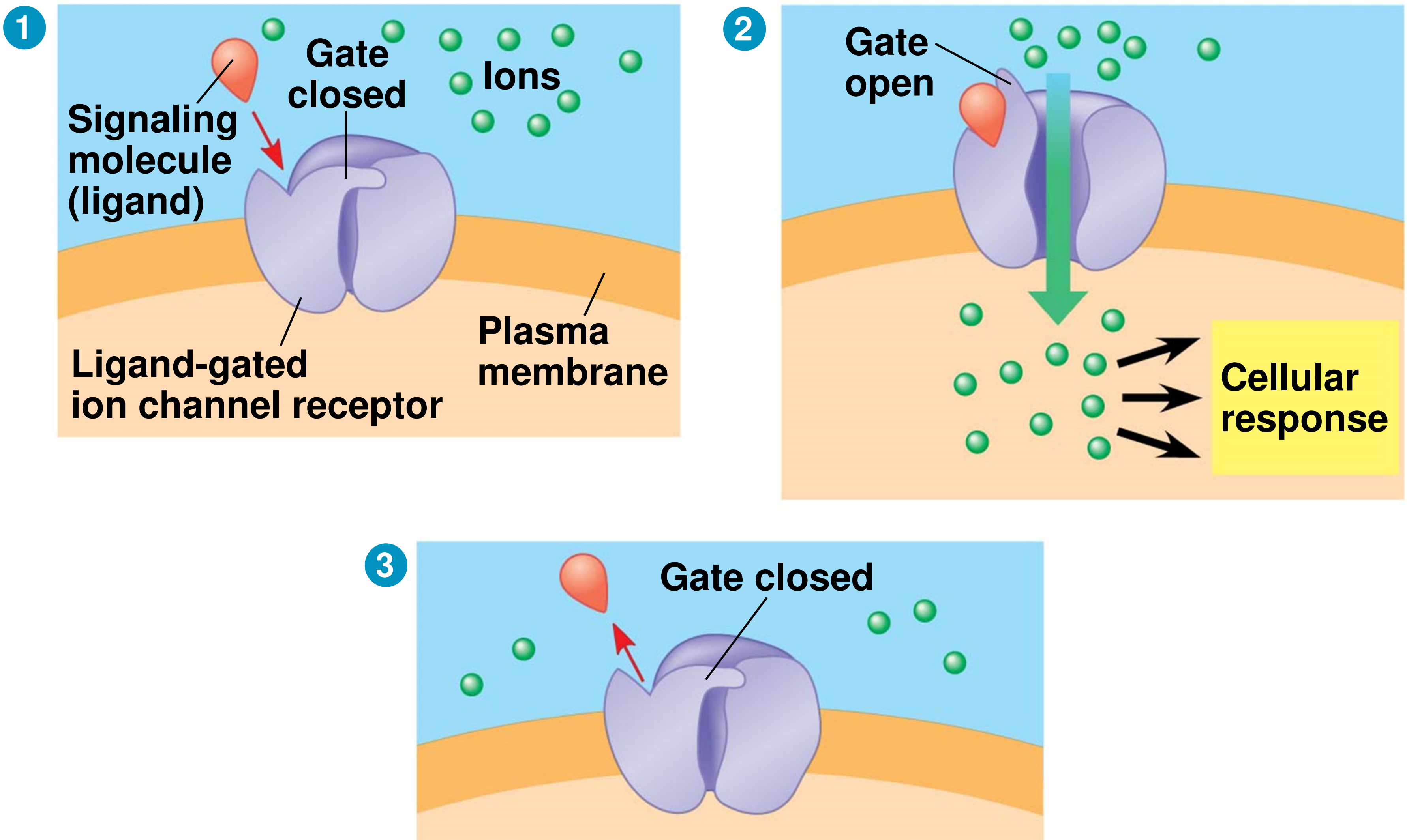
- **G protein-coupled receptors (GPCRs)** are plasma membrane receptors that work with the help of a **G protein**
- G proteins bind to the energy-rich molecule GTP
- The G protein acts as an on-off switch: If GTP is bound to the G protein, the G protein is inactive
- Many G proteins are very similar in structure
- GPCR pathways are extremely diverse in function

Figure 5.21-2


1
Activated GPCR
Signaling molecule
Inactive enzyme
Plasma membrane
GTP
Activated G protein
CYTOPLASM
2
Activated enzyme
GTP
Cellular response

- A **ligand-gated ion channel** receptor acts as a "gate" for ions when the receptor changes shape
- When a signal molecule binds as a ligand to the receptor, the gate allows specific ions, such as Na^+ or Ca^{2+}, through a channel in the receptor
- Ligand-gated ion channels are very important in the nervous system
- The diffusion of ions through open channels may trigger an electric signal

Figure 5.22-3

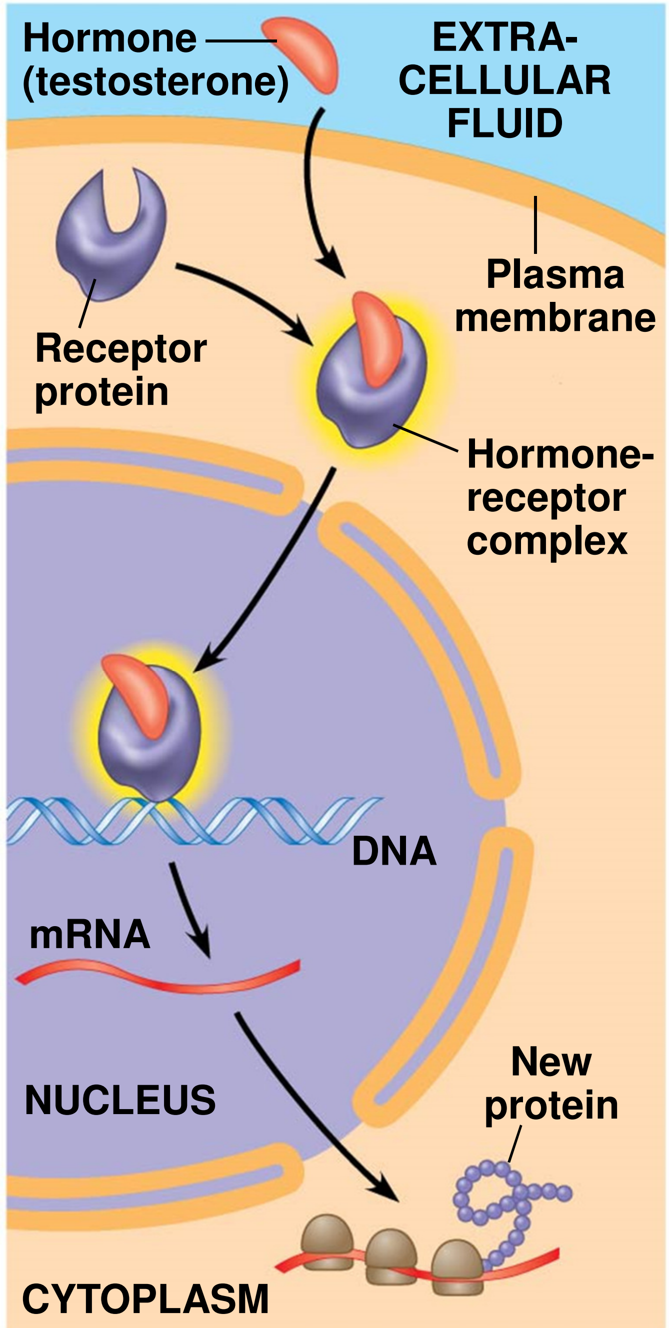


1
Signaling molecule (ligand)
Gate closed
Ions
Ligand-gated ion channel receptor
Plasma membrane
2
Gate open
Cellular response
3
Gate closed

Intracellular Receptors

- Intracellular receptor proteins are found in the cytosol or nucleus of target cells
- Small or hydrophobic chemical messengers can readily cross the membrane and activate receptors
- Examples of hydrophobic messengers are the steroid and thyroid hormones of animals and nitric oxide (NO) in both plants and animals
- When receptors are activated, they may act as *transcription factors*
  - Control which genes are turned on

Figure 5.23



Hormone (testosterone)
EXTRA-CELLULAR FLUID
Plasma membrane
Receptor protein
Hormone-receptor complex
DNA
mRNA
NUCLEUS
New protein
CYTOPLASM

Transduction by Cascades of Molecular Interactions

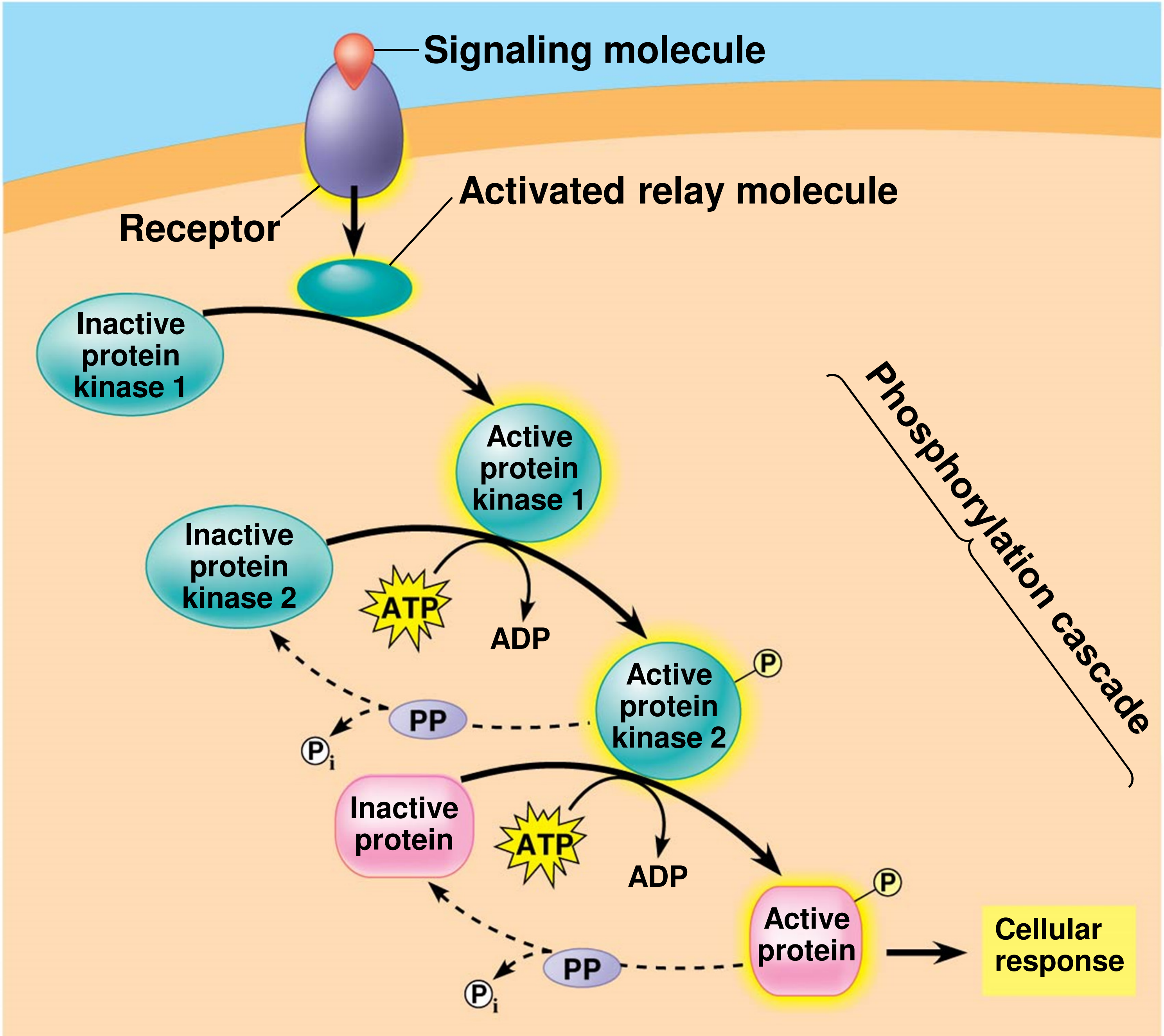
- Signal transduction usually involves multiple steps
- Multistep pathways can amplify a signal
  - A few molecules can produce a large cellular response
- Multistep pathways provide more opportunities for coordination and regulation of the cellular response than simpler systems do

- The molecules that relay a signal from receptor to response are mostly proteins
  - The interaction of proteins is a major them of cell signaling!
- Like falling dominoes, the receptor activates another protein, which activates another, etc., until the protein producing the response is activated
- At each step, the signal is transduced into a different form, usually a shape change in a protein

Protein Phosphorylation and Dephosphorylation

- Phosphorylation and dephosphorylation are a widespread cellular mechanism for regulating protein activity
- **Protein kinases** transfer phosphates from ATP to protein, a process called *phosphorylation*
  - Addition of phosphate groups
  - Often changes the form of a protein from inactive to active
- Regulate cell division

Figure 5.24



Signaling molecule
Receptor
Activated relay molecule
Inactive protein kinase 1
Active protein kinase 1
Inactive protein kinase 2
ATP
ADP
Active protein kinase 2
P
PP
Pi
Inactive protein
ATP
ADP
Active protein
P
PP
Pi
Cellular response
Phosphorylation cascade

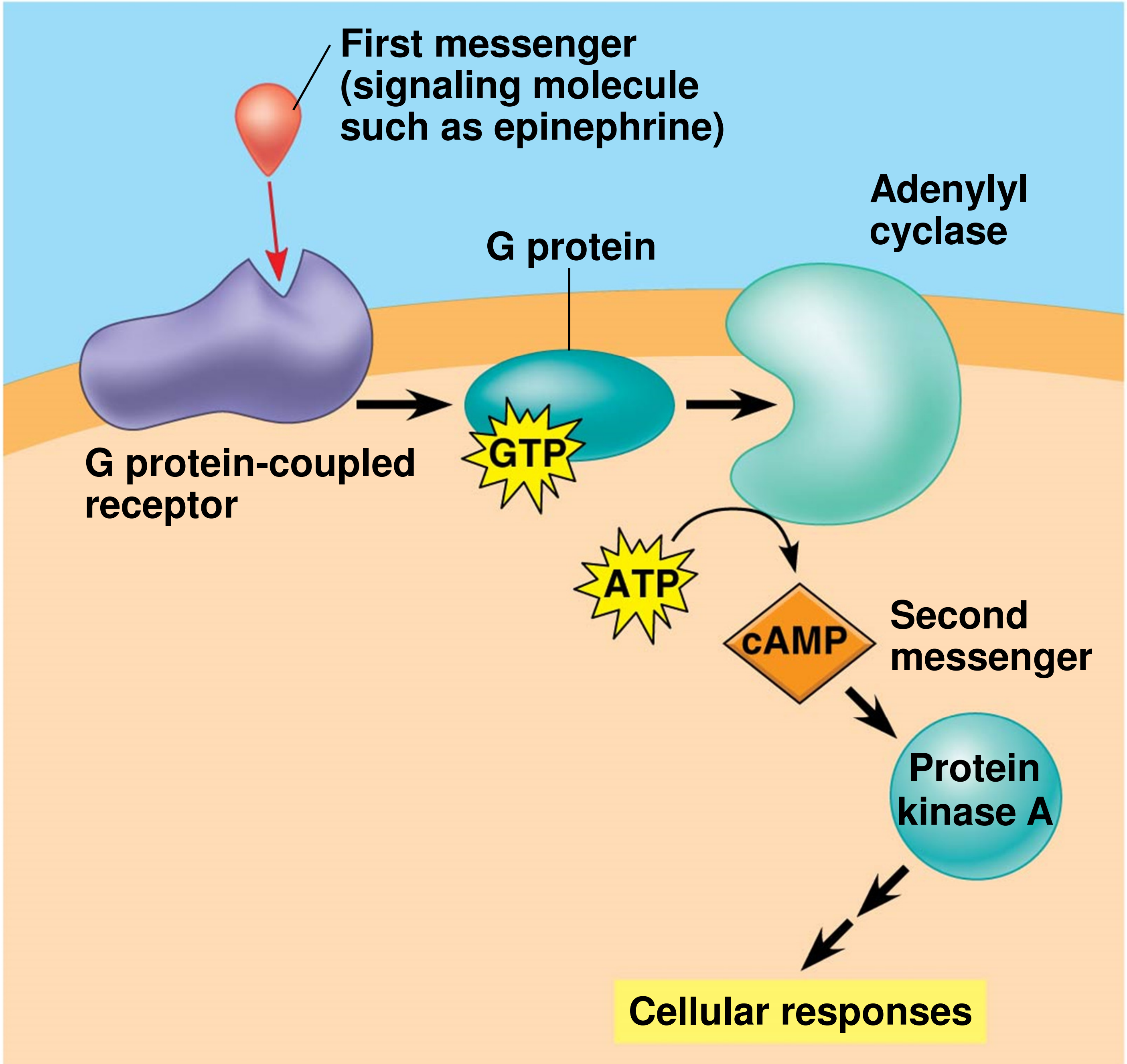
- **Protein phosphatases** remove the phosphates from proteins
  - Called *dephosphorylation*
  - Phosphatases provide a mechanism for turning off the signal transduction pathway
- They also make protein kinases available for reuse, enabling the cell to respond to the signal again
- Phosphorylation-dephosphorylation systems acts as a molecular “switch”

Small Molecules and Ions as Second Messengers

- The extracellular signal molecule (ligand) that binds to the receptor is a pathway's "first messenger"
- **Second messengers** are small, nonprotein, water-soluble molecules or ions that spread throughout a cell by diffusion
- Cyclic AMP and calcium ions are common second messengers

- **Cyclic AMP (cAMP)** is one of the most widely used second messengers
- Adenylyl cyclase, an enzyme in the plasma membrane, rapidly converts ATP to cAMP in response to a number of extracellular signals
- The immediate effect of cAMP is usually the activation of protein kinase A, which then phosphorylates a variety of other proteins

Figure 5.25

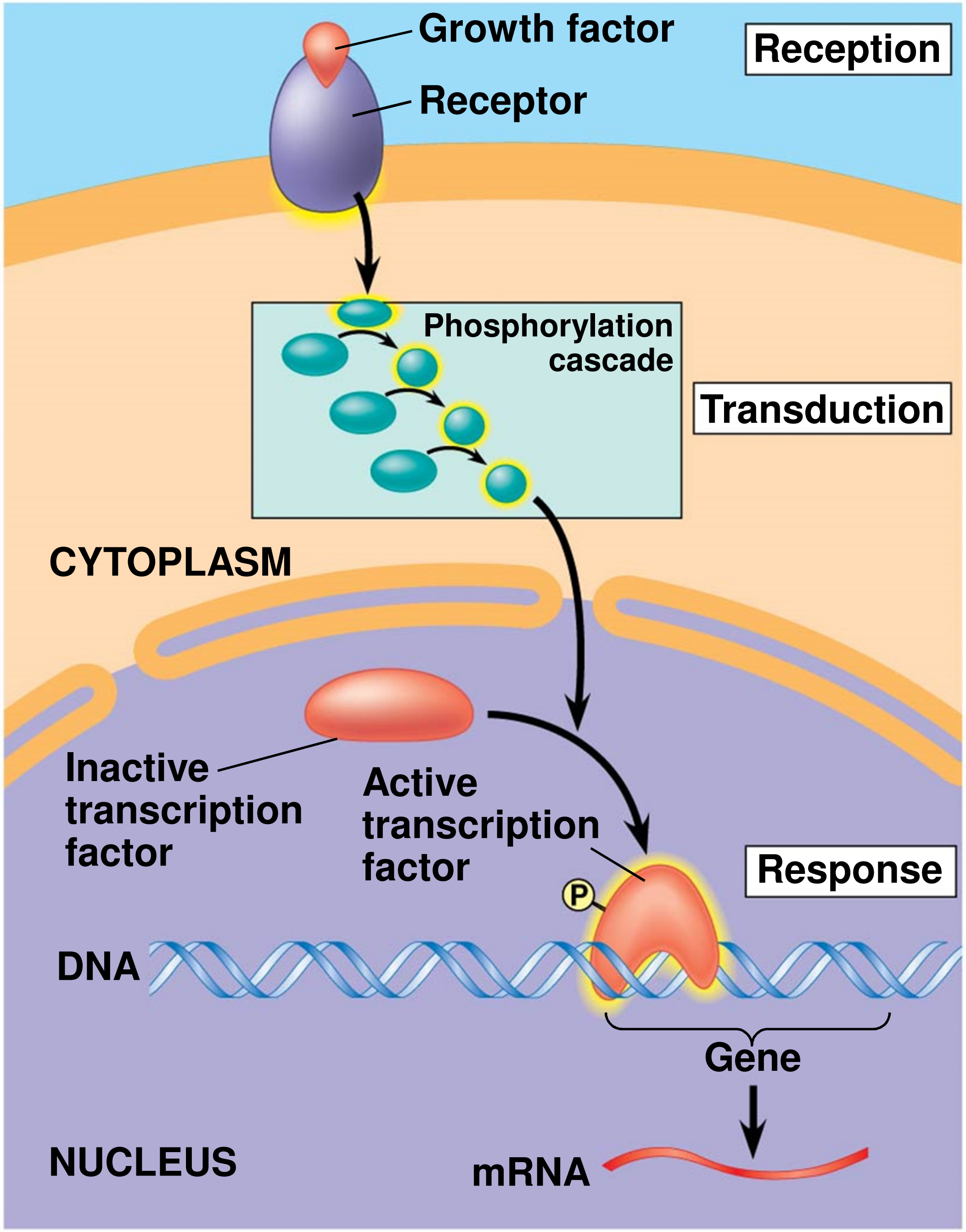


First messenger
(signaling molecule
such as epinephrine)
Adenylyl
cyclase
G protein
G protein-coupled
receptor
GTP
ATP
cAMP
Second
messenger
Protein
kinase A
Cellular responses

Response: Regulation of Transcription or Cytoplasmic Activities

- Ultimately, a signal transduction pathway leads to regulation of one or more cellular activities
- The response may occur in the cytoplasm or in the nucleus
- Many signaling pathways regulate the synthesis of enzymes or other proteins, usually by turning genes on or off in the nucleus
  - Sometimes a signaling pathway may regulate the *activity* of a protein rather than its *synthesis*
- The final activated molecule in the signaling pathway may function as a transcription factor

Figure 5.26


Growth factor
Receptor
Reception
Phosphorylation cascade
Transduction
CYTOPLASM
Inactive transcription factor
Active transcription factor
P
Response
DNA
Gene
NUCLEUS
mRNA

The Evolution of Cell Signaling

- Biologists have discovered some universal mechanisms of cellular regulation, evidence of the evolutionary relatedness of all life
- Scientists think that signaling mechanisms first evolved in ancient prokaryotes and single-celled eukaryotes
- These mechanisms were adopted for new uses in their multicellular descendants